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PATHOLOGICAL HISTOLOGY

VOL. I.

MANCHESTER MEDICAL SOCIE

MANUAL
OF
PATHOLOGICAL HISTOLOGY

BY

CORNIL AND RANVIER

MANCHESTER MEDICAL SOCIETY

SECOND EDITION, RE-EDITED AND ENLARGED

Translated with the Approbal of the Authors

BY A. M. HART

VOL. I.

GENERAL PATHOLOGICAL HISTOLOGY

LESIONS OF THE ELEMENTS AND TISSUES

WITH 284 FIGURES INTERSPERSED IN THE TEXT

LONDON
SMITH, ELDER, & CO., 15 WATERLOO PLACE
1882

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AUTHORS' PREFACE

TO THE SECOND EDITION.

THE first edition of this manual was published in three parts; the first in 1869, the second in 1873, and the third in 1876. It has been very favourably received by the French medical public, and the successive issues demanded have afforded us the satisfaction of seeing that we have succeeded in making the most important data of pathological histology part of the ordinary knowledge of students. The first edition is now out of date and no longer abreast of science, so that we have been obliged almost entirely to recast the work. The general account of normal histology placed at the beginning of the first volume has been remodelled and brought up to the level of the progress made in the last ten years. In this decennial period normal histology has made relatively greater progress than pathological histology, but the latter, which is based on the former, and which borrows from it not only its discoveries but its methods, has also undergone great changes. Thus in some chapters we have preserved nothing but the heading, and we have added many chapters which were not in the first edition. Many new illustrations have been added, and in every detail we have striven to make the second edition worthy of the success which attended the first. The entire work forms two volumes: the first contains the general pathological anatomy of the tissues; the second will include the pathological histology of the organs.

PARIS: *October* 25, 1880.

TRANSLATOR'S PREFACE.

In translating this standard treatise from French into English I have accomplished a task, the usefulness of which will, I believe, be generally acknowledged by students and others in England. In its simplicity of arrangement, its comprehensiveness and originality, the Pathological Histology of Cornil and Ranvier is acknowledged to have no rival. Only the first volume of the second edition is now presented. The second volume will follow in due course, and will be translated as soon as it is published in France. The translation closely follows the original; but, mindful of the needs, and to serve the convenience, of students, I have re-paragraphed the book, grouping under one heading all that is said on one subject, and for facility of reference I have headed the paragraphs with letters in Egyptian type. I have also compiled and added a complete index and a few notes.

The translation was undertaken with the concurrence of my master, Professor Ranvier, and of M. Cornil, they being the more desirous of an authorised English translation, as a translation of the first edition had appeared in America without their authority. The figures are from the same blocks as those used in the French edition.

I wish gratefully to acknowledge the kindness of Dr. Klein in reading and correcting the proofs for me as the book passed through the press.

London: *March* 14, 1882.

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PART I.
GENERAL PATHOLOGICAL ANATOMY.

CHAPTER I.

A SUMMARY OF NORMAL HISTOLOGY—CELLS AND NORMAL TISSUES.

I.—The Cell Theory and the Structure of Cells.

Before entering on the study of pathological histology, we propose in a few pages to give a summary of our present knowledge of normal histology, so that the reader may understand the principles which have guided us in our exposition of pathological facts.

Histology, founded by Bichat under the name of *General Anatomy*, took a fresh departure from the moment that Schwann, extending to animal tissues the discoveries Schleiden had made in the vegetable world, founded the *cell theory* (1839). From the researches of Schwann it was established that the cell, in the animal as in the vegetable world, is essentially the organic unit, the most simple body in which life is individualised, in such a manner that certain living individuals, vegetable or animal, possessing the functions of nutrition, motion, and reproduction, are composed of a single cell.

In beings of a more complex structure, cells are either surrounded by an intercellular substance which differs according to the nature of the tissues and organs, the cells being the essential part; or they are so greatly modified that they can scarcely be recognised unless the metamorphosis has been watched; here, again, cells play the principal part.

According to Schwann, the cell is composed of: 1, an enveloping membrane; 2, contents more or less liquid; 3, a nucleus; 4, one or more nucleoli contained within the nucleus. This conception and definition of a cell were accepted by the successors of Schwann, of whom the most illustrious were Remak, Reichert, Virchow, Kölliker, Donders, &c. These teachers, however, have completely modified Schwann's theories regarding cell-formation.

Schwann, in fact, admitted a *free formation* (spontaneous generation) in a primordial generative fluid, which is found alone, or situated between pre-existing cells (blastema or cytoblastema). In this fluid a granule appears; this is the rudiment of the nucleolus.

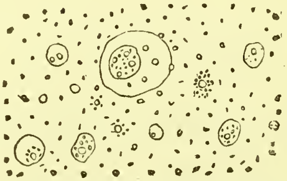

Fig. 1.—Diagram of the Development of Cells (after Schwann).

Around it new granules group themselves: these are inclosed by a membrane, and thus the nucleus is formed. The nucleus acts on the surrounding blastema, fresh granules appear, and soon become enclosed in a cellular membrane; from this moment is formed the complete element, called a *cell.*

Remak, whilst engaged in studying the phenomena of embryonic development, entirely reversed this theory, preserving, however, all that was fundamental in Schwann's conception of a cell. Starting from the idea that the ovule is a true cell, of which the vitelline membrane is the cell-wall, the vitellus the contents, the germinal vesicle the nucleus, and the germinal spot the nucleolus, he observed that all the cells of the embryo were derived from this cell, according to the following process: After fecundation the vitellus is divided by cleavage into two parts, by a second cleavage into four parts, and so on until a great number of spherical bodies are formed. These segmented balls, or new cells, apply themselves to the internal surface of the vitelline membrane so as to form a layer (the blastoderm), which soon divides into three laminæ composed entirely of cells. It is from these cells, by a process of which segmentation is always the essential characteristic, that all cells, according to him, are produced. After investigations into the origin of all tissues from these embryonic cells, Remak concluded that every cell was produced from a pre-existing cell by one of three different methods: by segmentation or scissiparity, by germination or budding, or by endogenous formation. At the present time, according to the conception of the cell we shall presently unfold, these three methods cannot be looked upon as essentially different.

Virchow applied to pathological anatomy the data furnished by Remak concerning physiological development. He considered that every new formation of cells, or every neoplasm, is the result of a continuous development from pre-existing cells; and he thus tightened the bonds uniting pathology and physiology. Like Remak, he adopted Schwann's definition of a cell, recognising in it a cell-wall, contents, a nucleus, and nucleolus.

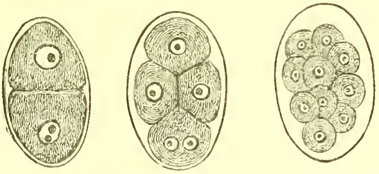

FIG. 2.—SEGMENTATION OF THE OVULE IN ASCARIS NIGROVENOSA.

(Figure borrowed from Kölliker.)

Subsequently, owing to the labours of Max Schultze, Recklinghausen, Kühne, L. Beale, &c., the definition of a cell was considerably modified.

It is long since Dujardin first observed that the lowest order of beings composed of a single cell were not always enveloped by a membrane, and composed of a substance insusceptible of changing shape, inasmuch as very extensive processes could be sent out from it. Dujardin called this substance *sarcode*, and its movements *sarcodic movements*. Max Schultze, investigating the same phenomena more completely, observed these movements not only in the unicellular animals called amœbæ, but also in the cellular elements of more complex animals. He compared the animal cellular masses, susceptible of movement, to the vegetable cellular masses long known under the name of *protoplasm*, and called the fundamental substance of animal cells also by the name of *protoplasm*, and the movements of which it is capable *amœboid movements.*

A very large number of the cells in the higher animals and in man, white blood-corpuscles and embryonic cells for example, are composed of protoplasm, have no cell-wall, and show amœboid movements. In order that the truly characteristic movements of protoplasm may be observed, cells should be placed in the same medium and under the same conditions of humidity and temperature in which they exist in the normal state. In cold-blooded animals the phenomenon is observed very easily, as conditions of temperature may be disregarded. All that is necessary is to take the blood of a frog or triton, and to examine it, taking care to prevent evaporation. Protoplasmic processes are seen to be pushed out from the periphery of the white blood-corpuscles, and to ramify in such a manner that expansions arising from the same cell, and coming in contact with others, they are often fused together; little by little the entire mass of protoplasm may pass into a process, thus causing the body of the cell to become displaced: the process may also sometimes be seen to be withdrawn and to melt away into the common mass. If coloured particles are in the neighbourhood of the cells showing these movements, they are absorbed into the amœboid process, and may thus penetrate into the interior of the cell.

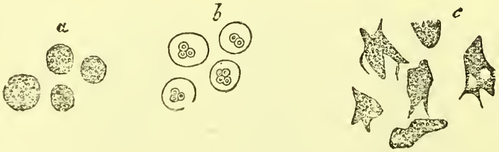

FIG. 3.—PUS CELLS.

a, seen in a neutral fluid; *b*, seen after the action of water or acetic acid; *c*, living cells showing amœboid movements.

Fusion of the amœboid processes, and penetration of coloured particles into the interior of the cell, prove that the cell possesses no membrane. These facts alone suffice to destroy the definition of a cell given by Schwann and accepted by Remak and Virchow. Nevertheless it is not contended that every cell is destitute of a cell-wall; but that, when this exists, it constitutes only an accessory part of the cell.

The definition of a cell is thus reduced to *a mass of protoplasm enclosing a nucleus.*

The nucleus of the cell seems to be a vesicle, the enveloping membrane of which is often made evident by a double contour. The contents are sometimes clear, sometimes slightly granular. The high refraction of nucleoli has given rise to the idea that they may be composed of fat; but the facility with which they are coloured with carmine, and their solubility in liquor potassæ, show that we have not here to do with fat, which is not coloured with carmine, and does not dissolve in cold liquor potassæ. Further, the researches of Balbiani on the ovule demonstrate that the germinal spot, of a size large enough to be studied, is a vesicle capable of change of shape and size under the eye of the observer. We shall also see, later on, that, with regard to the epithelial cells of the skin, nucleoli are capable of becoming vesicular under even slight irritation. Originally every cell is simply composed of a mass of protoplasm surrounding a nucleus. Among all the cells possessing this initial structure no differences have been observed indicating that a given cell will undergo certain ulterior changes. In the adult animal, cells of this simple structure are only found in the blood (white corpuscles or lymph cells), or in tissues subject to constant renovation; but they constitute the entire embryo, and thus deserve the name of *embryonic cells*. Cells which have no cell-wall, and which are composed of a protoplasm capable of amœboid movements, are—1, embryonic cells before they have taken any determined form; 2, the cells in the developing layer of the medulla of bone; 3, the mother-cells found in the same spot; 4, the white corpuscles of the blood. Embryonic cells of a mean diameter of 10 μ to 15 μ[1] are composed of an irregular mass of granular protoplasm, and are generally of a spherical form. The protoplasm swells on the application of water or acetic acid, and is coloured dark brown with a solution of iodine, and feebly with carmine, which latter renders its granular condition more apparent. This mass encloses an ovoid or spherical nucleus, which is often not visible till after death, or till acted upon by water or acetic acid. The nucleus generally shows a double contour, and contains one or more nucleoli. In the place of one nucleus, if the element be losing its vitality, there are often seen several little angular nuclei resembling small fragments, such as are formed in pus cells undergoing caseous degeneration. If the cells are growing, the nuclei are spherical and well developed.

In the developing layer of bone from cartilage, cells are met with presenting such close analogies to embryonic cells, that we know of no characteristics sufficient to distinguish them. These cells subsequently undergo modifications which slightly differentiate them from the primitive type.

---

[1] We take as the unit of microscopic measurement the thousandth of a millimetre and represent it by the letter μ.

The multi-nucleated cells which are met side by side with them possess the same general properties, with the exception of the multiplicity of their nuclei, the great irregularity of their shape, and the buds which they throw out; the protoplasmic material of which they are composed shows identical reactions. Later on these elements become flattened, more consistent, and diverge from the original type.

Embryonic cells, as well as lymph cells of the blood and lymph, which are of like structure, habitually contain glycogenic matter in a notable quantity. In fact, when acted on by iodine in a solution of iodide of potassium, these elements are stained a diffuse violet colour, or they present in their interior little drops of the same colour. We are justified in the present condition of science in considering this reaction as characteristic of glycogenic matter. The researches of Claude Bernard have, moreover, taught us that most of the embryonic tissues, when in a state of great activity of development, contain glycogenic matter in their cells. The most remarkable example of this presence of glycogenic matter is afforded us in the striated muscular tissue of the embryo. The primitive bundles are composed of cylinders of which the

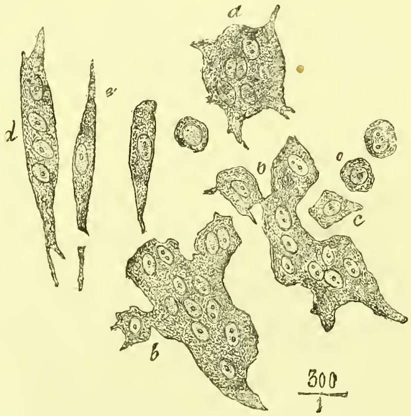

Fig. 4.—Cells of the Medulla of Bone undergoing Development.

a, Mother-cell with multiple nuclei and processes; *b*, the same elements showing buds about to separate; *c*, young cells with a single nucleus identical with embryonic cells; *d*, a mother-cell seen sideways; *e*, a fusiform cell with a single nucleus.

periphery alone is striated, whilst the central formative protoplasm is not. The glycogenic matter is stored up only in this protoplasm. In coryza also, at its commencement, the lymph cells which escape with the serous effusion contain glycogenic matter, whilst the ciliated cylindrical cells, even those which are broken up into fragments still provided with cilia, do not contain glycogenic matter.

If we leave aside the early phenomena of the development of embryonic cells investigated by Bütschli, Auerbach, Balbiani, Fol, &c., to occupy ourselves especially with the growth and multiplication of cells after their production, we shall find in the lymph cells of the axolotl and proteus, examined in their living state, remarkable examples of multiplication of cells by division. If the lymph cells of the blood of these animals be observed in their own plasma, and without the addition of any reagent, the nuclei which they contain may be seen quite distinctly, whilst in the frog and in mammals no nucleus can be distinguished in similar cells when alive and in a state of physiological activity.

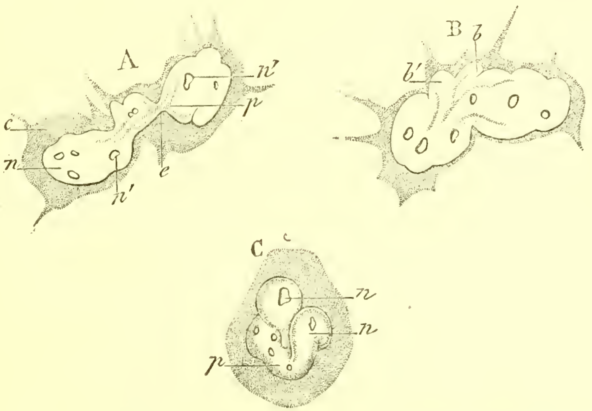

Fig. 5.—Lymph Cell of the Blood of Axolotl examined in the Living State.

A, cell at the beginning of the observation; *c*, protoplasm with its amœboid processes; *n*, the nucleus constricted at *e*; *n′*, nucleoli. B, the same cell observed at the end of twenty minutes; the nucleus is enlarged at the middle and is sending out two buds, *b*, *b′* C, the corpuscle treated with a 33 per cent. solution of alcohol; *p*, nucleus with its buds *n*, *n′*.

A drop of blood of the axolotl, obtained by an incision either in the membranous expansion of the skin or in the gills, should be placed in the centre of a moist-chamber slide, evaporation being prevented by a border of paraffin round the edge of the coverglass. Among the red corpuscles, the white blood-corpuscles, recognised by their rounded form, their smaller diameter, and by the absence of hæmoglobin, are soon seen to send forth little amœboid processes, the form and size of which vary incessantly. In the midst of the protoplasm the sharp outline of the nucleus is perceived. It is round, irregular, or elongated in shape, or often folded on itself. The form of the nucleus varies according to the amœboid activity of the protoplasm which surrounds it. Whilst engaged in following one of these cells in its changes of form, and in its migrations, it may chance to divide under the eye of the observer. The nucleus, at first distorted in a thousand different ways by the pressure of the moving protoplasm, finally divides into two distinct nuclei contained within the same cell. The cell, itself participating in turn in the process of division, is either divided by a line of segmentation, or retracts centrally till separation is completed.

Nuclei of the lymph cells of the blood and of the lymph are often elongated, and folded on themselves, affecting a serpentine form. If fixed by the action of dilute alcohol or by the vapour of osmic acid, and then coloured with picro-carmine or with aniline red, their true shape can be accurately ascertained. It is then easy to understand how that cells containing one elongated nucleus folded on itself have often been described as multinucleated cells.

In the process of multiplication of lymph cells the amœboid activity of protoplasm plays an important part. In the multiplication of the cells of tumours, the multiplication of the nuclei which precedes that of the cells seems to depend principally on a process of change which takes place in the nucleus itself.

All embryonic cells have the property of producing elements similar to themselves by the following process: the nucleus enlarges, the nucleolus becomes constricted and divides; the nucleus soon also divides, either by cleavage, which cuts it in two, or by a kind of constriction which gives it the shape of an hourglass. The protoplasmic mass surrounding the two new nuclei then divides, and two cells are the result. The segmentation of the protoplasm does not always follow that of the nucleus, so that a large number of nuclei may be contained in the same cell (*a*, *b*, fig. 4). A portion of protoplasm may not unfrequently be seen to become detached enclosing a nucleus (*b*, fig. 4).

Embryonic cells are either destroyed, or undergo a series of changes which give them the characteristic appearances found in the different tissues. The simplest example of modification of embryonic elements is that in which there is an elaboration, within the protoplasm, of substances which did not exist there before; for example, in the first stage of the formation of fat cells, minute drops of fat may be seen in the protoplasm. In other cases pigment granules are found, for example in the cases of cells contiguous to red blood-corpuscles which have been extravasated into a tissue. The most important modification which embryonic cells undergo is in the formation of a membrane enclosing the protoplasm. This membrane is comparable to the secondary membrane of vegetable cells where it is composed of cellulose, whilst in animals it is composed of an albuminoid substance: such are fat cells, cartilage cells, &c. In every kind of cell there are striking differences with regard to this membrane. It is still disputed whether it is produced by thickening of the superficial layers of the protoplasm, or by secretion of the latter. Whichever it may be, it is entirely distinct from the protoplasm, and capable of being isolated from it. This can be well observed in fat cells, cartilage cells, and the epithelial cells of the buccal mucous membrane. To demonstrate this fact in the latter a 40 per cent. solution of potash should be employed. From the moment that a cell is surrounded by a secondary membrane, or that a substance, more often elaborated by itself, is formed at its periphery, it is fixed in a permanent form. It then assists in the construction of a tissue, so that it is impossible to study cells without considering the tissues which contain them. Hence we shall study cells in considering the tissues.

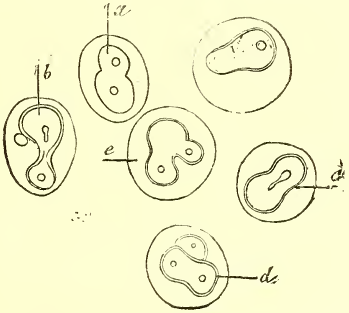

Fig. 6.—Various Phases in the Division of the Nucleolus and Nucleus in Cells from Sarcoma in a Horse.

a, nucleus already constricted and having two nucleoli; *b*, division more advanced; *c*, nucleolus about to undergo division; *d*, *e*, various forms of segmentation of the nucleus. Magnified 450 diameters.

II.—NORMAL TISSUES.

Normal tissues may be divided into three groups.

GROUP I. Those in which the substance uniting and separating the cells is characterised by its form, its physical and chemical properties (connective, cartilaginous, and osseous tissues). In these tissues, though the cells have special physiological properties relating to the formation and preservation of the tissues, their form is not characteristic when considered separately.

GROUP II. The second group comprises those tissues in which the cell has undergone such modifications that it has generally become unrecognisable as a cell, but has assumed certain fixed physical, chemical, and physiological characters. These are the muscular and nervous tissues.

GROUP III. This includes tissues composed of cells having a regular and constant evolution. They are closely bound together by a cementing substance very slight in quantity. Of such are glandular and investing epithelium. Their cells have often a characteristic form, and they elaborate certain fixed substances; thus, the epidermal cells elaborate horny matter; certain mucous cells, mucin; certain glandular cells of the stomach, pepsin, &c.

GROUP I. **Connective, Cartilaginous, and Osseous Tissues.**

Connective Tissues.—The connective tissues are the mucous, areolar, fibrous, adipose, retiform, and elastic tissues.

The formation of **mucous tissue** from embryonic tissue is very simple. In the simplest variety of this tissue, that met with in the vitreous humour, a hyaline substance containing a large quantity of mucin is thrown out between the cells, these remaining quite independent of one another. In another variety, that of the umbilical cord, the cells become fusiform or stellate and anastomose, a gelatinous substance being formed between them. In the midst of this gelatinous material little bundles of connective tissue, recognised by their fibrous structure and their wavy form, are gradually developed. These bundles increase in diameter progressively as they develop. As to the cells, they are always formed of a mass of protoplasm containing one or more nuclei. Rounded cells, composed also of a mass of protoplasm, are frequently seen beside the stellate cells.

The cells which form the constituent elements of **areolar tissue** are also derived from embryonic cells. Between them are bundles of connective tissue, which, but slightly developed in mucous tissue, are here greatly increased. They are very numerous, and the larger number of them are of a considerable diameter. The bundles are made up of fibrils held together by a soft cementing substance which permits them to glide one over the other. It is this which gives them their undulating appearance, resembling hair. Connective-tissue cells are never seen in the interior of a bundle, but always on its surface. They are flat, branching, and often have equally flat processes which unite them with one another, as in mucous tissue. On their surfaces ridges are often seen, caused by the impression of neighbouring bundles—ridges which, recently described by Waldeyer, are analogous, but not similar, to those one of us described in tendons. These cells have one nucleus, which is also flat.

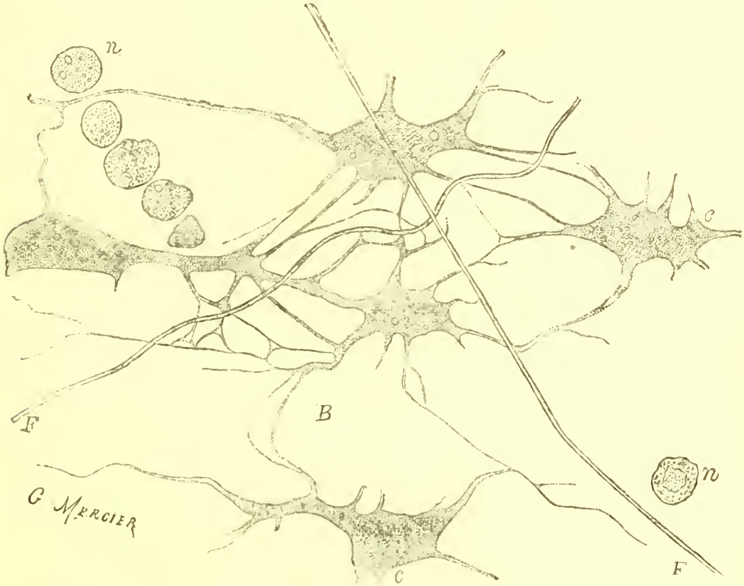

FIG. 7.—MUCOUS TISSUE OF THE UMBILICAL CORD OF THE EMBRYO OF THE SHEEP.

c, ramifying cells; n, embryonic or lymph cells; F, bundles of connective tissue; B, amorphous material. Magnified 500 diameters.

In the first edition of this manual we adopted Virchow's view, modified by Recklinghausen, as to the structure of connective tissue. We thought then that this tissue was formed of a fundamental fibrillar substance, in the midst of which canals were hollowed out (plasmatic canals, serous channels) and that the plasmatic or connective-tissue cells were included within these canals. This false interpretation arose from the fact that connective tissue was generally examined in transverse sections after desiccation or hardening in chromic acid or alcohol, and after the action of acetic acid. But Henle, who, in studying connective tissue, continued to have recourse to dissociation, always declared himself against the teaching of Virchow and his pupils. His description of connective-tissue bundles is perfect. He recognised their fibrillar structure, and described the annular and spiral fibres which are twisted round the fasciculi, lacing them together and consolidating them. Henle, however, was not aware of the existence of active cells, so that, according to him, connective tissue only contained elements derived from primitive cells, and which he called fibres of nuclei (annular, spiral, and elastic fibres). Annular and spiral fibres are stained red with carmine, and retain their colour after the addition of acetic or formic acid, whilst elastic fibres remain colourless. The nuclei of connective-tissue cells, and the surface of the bundles, are stained with carmine exactly as the spiral fibres. Virchow, who recognised the existence of the nuclei, considered that they were contained within cells analogous to osseous corpuscles, in that they are necessarily limited by the surface of the fasciculi, which are also distinguished by their colour.

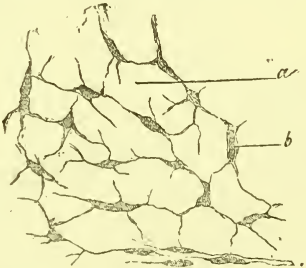

Fig. 8.—Connective Tissue.

a, connective-tissue bundles cut transversely or obliquely to their direction ; *b*, connective-tissue cells. Magnified 200 diameters. Section obtained after desiccation, stained with carmine and treated with acetic acid.

Although Virchow was mistaken in the form, the relations, and the signification of the connective-tissue cells, yet to him nevertheless is due the merit of having affirmed their existence.

To understand the structure of connective tissue, that is to say, the form of its cells and the relation of these cells to the bundles of fibres, simple dissociation in water, as was formerly done, and as Henle practised, is not sufficient. In fact, if a small portion of subcutaneous tissue, taken from the human subject or a mammal, be dissociated in water with needles, the bundles are confusedly mixed together, so that it is difficult to distinguish one from the other, and to see what occupies the spaces between them. This tissue can only be studied by means of interstitial injections. The method of procedure is as follows: With a hypodermic syringe provided with a pointed cannula, a fluid such as serum, simple or feebly iodised, or a solution which has the property of fixing the delicate elements (nitrate of silver $\frac{1}{1000}$, osmic acid $\frac{1}{100}$, alcohol $\frac{1}{3}$, water $\frac{2}{3}$) is injected. A bulla of artificial œdema is produced, which increases in size as more fluid is injected, without its shape being notably modified. From this bulla thin sections of œdematous tissue are cut by very sharp scissors, and deposited at once on a slide and covered by a cover-glass. In preparations thus made, large, membranous, branching connective-tissue cells can be recog-

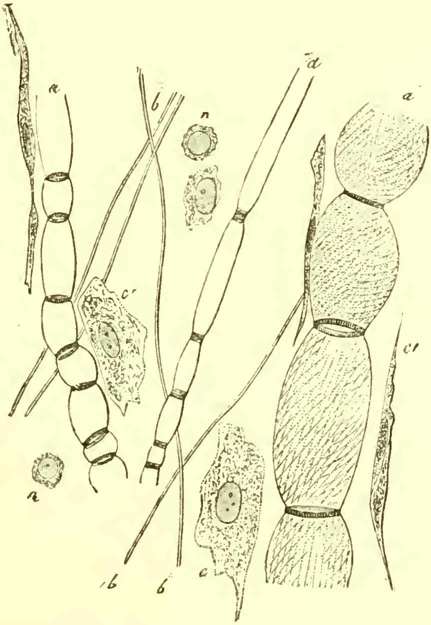

Fig. 9.—Subcutaneous Cellular Tissue from the Inguinal Region of the Dog.

a, connective-tissue bundles swollen by the action of formic acid and showing annular fibres; *b*, elastic fibres; *c*, flat connective-tissue cells seen full face; *c′*, the same seen sideways; *n*, lymph cells.

nised, and alongside them connective-tissue bundles, elastic fibres, and lymph cells. These latter do not occupy a fixed position in the tissue. They belong to the plasma which fills up the meshes between the fibrous bundles.

Lymph cells are capable, like all similar cells, of amœboid movements. When alive, and under favourable conditions, they give origin to protoplasmic processes, which implant themselves on neighbouring surfaces, are then withdrawn, whilst other amœboid or pseudopodic processes are formed, grow, and attach themselves like the first. It is by this mechanism that lymph cells move and travel. Thus they are essentially migratory elements, even though they are not carried along by any current of fluid. The migration of cells from the very centre of the tissues was discovered by Recklinghausen, and it has become a fact of considerable pathological importance.

Areolar tissue may be looked upon as mucous tissue in a more advanced stage of development. Thus, in the embryo where eventually connective tissue is formed, mucous tissue exists. At birth the umbilical cord and the vitreous humour are the only parts which remain as mucous tissue.

Into **fibrous connective tissue** (ligaments, aponeuroses, and tendons) the same constituent elements enter as into areolar tissue, that is to say, connective-tissue bundles, elastic fibres, and flat cells, only that the fasciculi, instead of lying, as in the areolar tissue, in every direction, and being up to a certain point independent of one another, are here parallel, or crossed in a simple manner in planes which are either perpendicular or more or less oblique. If parallel, the flat cells situated on their surface are arranged in rectilinear series, and bear impressions, more or less numerous and parallel, of other connective-tissue bundles pressed against their surface. When the fasciculi are perpendicular to one another, as in certain aponeuroses of the frog, for example, in that of the triceps cruralis, between the two layers of fibres flattened cells are noticed, having ridges formed by pressure corresponding to the interstices of the bundles, which are perpendicular to one another, some corresponding to the superficial plane of fibres and others to the deeper. In tendons, ligaments, and aponeuroses, lymph cells are not met with, and the plasma which bathes the constituent elements does not contain formed elements.

Adipose tissue results from an accumulation of fat within the cells of mucous or areolar tissue. The fat forms distinct granules in the midst of the protoplasm of the cell. Little by little these granules become larger, and they melt into one another. The nucleus is displaced towards the periphery. A secondary membrane is formed which completely envelops the element, so that a fat cell fully developed is formed of three distinct parts, externally an enveloping membrane, beneath it a layer of protoplasm containing the nucleus of the cell, and within a large drop of fat. In man, fat is fluid at the ordinary temperature of the body; after death, needles of margarin are developed in it. Connective-tissue cells which have become adipose cells are not arranged in a chance manner in connective tissue; they form groups, lobules of variable size possessing a distinct and very characteristic capillary network, each vascular mesh containing one or more fat vesicles.

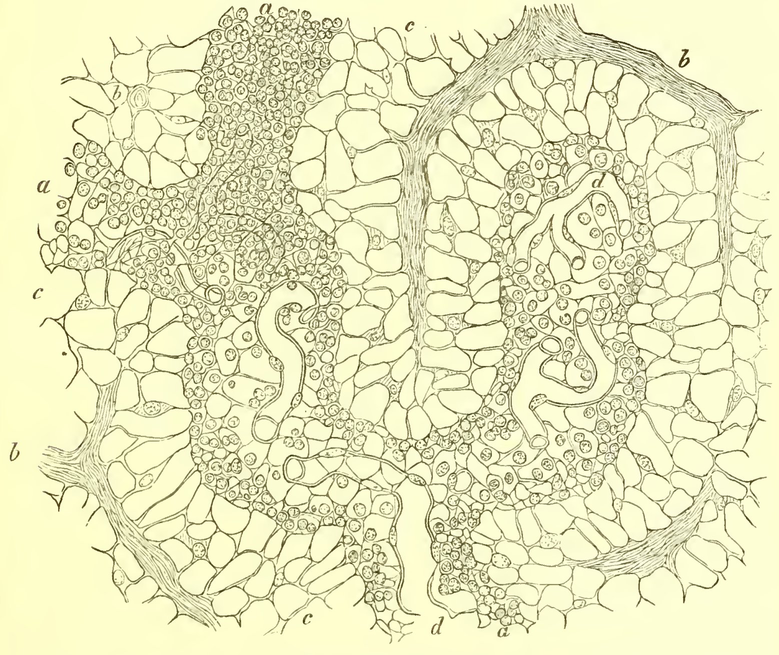

Fig. 10.—Section of the Medullary Substance of a Lymphatic Gland of the Ox.

a, follicular substance; *b*, fibrous trabeculæ; *c*, lymph channels; *d*, blood-vessels. Magnified 300 diameters. Figure taken from Recklinghausen.

In **retiform tissue** the fibres of connective tissue are extremely fine. They adhere together, then separate to unite with other fibrils, forming by their union a delicate reticulum, the trabeculæ of which pass in every direction, and are covered by flat delicate cells spread out on their surface and moulded on them like a varnish. The meshes of retiform connective tissue are traversed by vessels, and are filled with a plasma charged with lymph cells. Retiform connective tissue is found in the lymphatic glands, in the spleen, in Peyer's patches, &c.

Elastic fibres are found more or less in areolar tissue, and in fibrous tissue, but they only form an accessory part of these. The yellow ligaments found between the vertebral laminæ are, on the contrary, entirely formed of elastic tissue. Elastic fibres, of which the diameter varies, produce by anastomosing with one another a reticulum of different-sized meshes. In the yellow elastic tissue the fibres are voluminous, cylindrical, and frequently anastomose. In the large arteries elastic tissue forms the fenestrated membrane (the internal elastic layer and the middle coat of the aorta and carotid), the openings of which are of variable size, whilst in areolar tissue the meshes of the elastic tissue are so large that it is difficult to trace the network which they form. Elastic fibres, like connective-tissue bundles, are developed in the intercellular substance between the embryonic cells and connective-

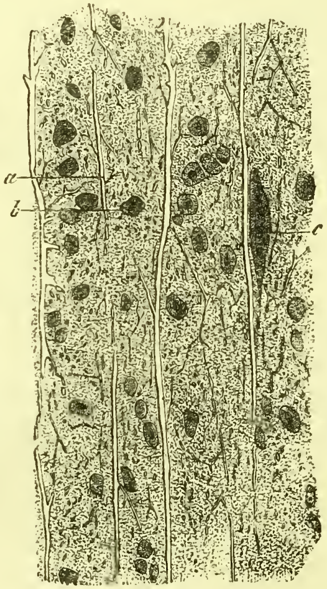

Fig. 11.—Longitudinal Section of the Human Aorta.

a, elastic layer; *b* and *c*, muscular fibres.

tissue cells already formed; if the cells take any part in their development it is simply an indirect one.

In all the various kinds of connective tissue which have been described, the cellular elements are at the commencement more or less globular; their protoplasm is succulent and their nuclei are well defined, but in the course of development these elements become thinner, dry up, so to speak, and it is then only that they take the form of laminæ. It will be shown hereafter how that irritation is sufficient, by increasing their nutrition, to bring the connective-tissue cells back to their primitive form.

Cartilaginous Tissue.—Cartilaginous tissue, like connective tissue, is found in the organism under different forms; but we always find in it one essential characteristic, that it is composed of cells completely surrounded by cartilaginous substance, that is to say, by a transparent substance which yields chondrin on boiling. The true **cartilage cell** is a mass of protoplasm containing a nucleus; its volume and form are very variable, even in the same kind of cartilage. Its diameter varies between 6 μ and 30 μ. In living cartilage the form of the cell is spherical, ovoid, or lenticular, but, when observed under the conditions in which an examination of cartilage is generally made, that is to say, after the addition of water, acetic acid, and other reagents, the cartilage cell assumes the most varied forms. Frequently fat granules or droplets of fat accumulate in the protoplasm of cartilage cells, but, even when fat is in such abundance that the cell might be called a fat cell, the nucleus persists, is well developed, and is always to be found alongside the drop of fat. It is spherical or slightly oval in form, and is bounded by a double line; the nucleoli are well defined. This slight description of the cartilage cell is based on numerous examinations made by means of a saturated solution of picric acid, a reagent which at the beginning of its action does not cause retraction of the protoplasm of the cartilage cell, and enables the nucleus to become apparent. A 1 per 200 solution of alum makes a still better reagent, in that it definitely fixes the cartilarge cell in its natural shape. The nucleus can be afterwards stained with a solution of purpurin. The cartilage cell has no peculiarity sufficient to distinguish it when isolated, and it is only because it is found in the cartilaginous tissue that the name cartilage cell has been given it. This cell cannot therefore be defined by its physical characters; it is solely distinguished by the property which it possesses of secreting cartilaginous material around itself.

In embryonic development, when cartilaginous tissue is about to appear, the embryonic cells are separated from one another by a substance, soft at first, which afterwards becomes more consistent and has all the characters of cartilaginous substance. At first, this substance exists in small quantity, but it soon increases and condenses in the form of a capsule round the cell. The capsule may also be produced by a new elaboration of the cell itself. Such is the *embryonic variety of cartilage* in which the cells and capsules are small and spherical. Soon the cells begin to multiply, and this is also one of the methods of the growth of cartilage. At this period it is not rare to observe two nuclei in one cell, and sometimes even the division of the nuclei may be observed. The nucleus enlarges and elongates, becomes constricted in the centre, and separates completely into two distinct elements. The division of the protoplasm is always consecutive to that of the nucleus, so that cells may be seen with two nuclei. Each of the new cellular masses has the property of elaborating around itself cartilaginous substance. Thus two secondary capsules may be produced within the primitive cell. In multiplying thus the cells are pressed one against the other, and become elongated and prismatic in shape. *Fœtal cartilage* is of this kind.

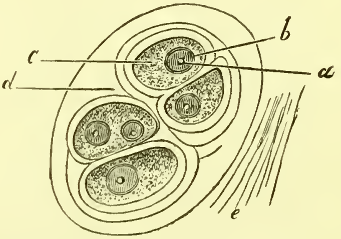

FIG. 12.—CARTILAGE CELLS ABOUT TO PROLIFERATE.

c, protoplasm of the cell; *a*, nucleolus; *b*, nucleus; *d*, primitive and secondary cartilaginous capsule; *e*, matrix. In one of the cartilage cells are two nuclei.

When the nutritive process is very active, the cells become larger and take a globular form, as is seen in cartilage undergoing ossification. Owing to the large size of these cells, all the phases of their development can be easily studied (fig. 12).

Permanent cartilage of the adult is composed of medium-sized cells which often contain secondary capsules. At the surface of the articulations and under the perichondrium they become changed in shape; the capsules are here lenticular and flattened in the direction of the surface, and contain no secondary capsules.

In the adult, whenever cartilage is in contact with bone, calcareous infiltration is observed in its deeper parts. This incrustation forms a perfectly regular layer in which cartilage cells are preserved. Calcareous infiltration causes such a change in cartilaginous substance that even after complete decalcification by means of an acid (hydrochloric or chromic) this layer remains condensed and perfectly distinct. This is *calcified cartilage.*

In individuals advanced in age the cells of the costal and thyroid cartilages show fatty infiltration, and the matrix mucoid degeneration. Owing to these changes irregularly shaped cavities are formed filled with mucus and fat granules. Sometimes calcareous infiltration is present at the same spot. Finally Virchow, after treating these parts with a solution of iodine alone, or followed by the action of sulphuric acid, observed that the cells give a red mahogany colour, and has hence described this change under the name of amyloid degeneration. Rapidly proliferating cells in cartilage undergoing ossification give a violet colour with a solution of iodine in iodide of potassium. This colour is owing to the presence of glycogenic matter in the protoplasm of the cartilage cells, the same as is met with in every cell that is in an active state of growth or proliferation (see p. 6).

In the centre of the intervertebral discs, and other symphyseal ligaments, a mucous substance is found in which either isolated cartilage capsules, or systems of capsules nested one within the other, exist. The protoplasm and the nucleus of a cartilage cell are found in the isolated capsules, or in the most internal of the nested capsules. This kind is called *mucous cartilage.*

The matrix which separates the cartilage capsules shows in certain places, as in the fibrous portion of the symphyseal ligaments, all the characters of fibrous tissue. Here the capsules are quite distinct from the matrix, and often contain secondary capsules. This is *fibro-cartilage.*

In the cartilages of the ear, in the arytenoid and the epiglottis, there is a cartilaginous tissue with well-defined capsules separated from one another by a reticulum of elastic fibres resembling felt. This is called *elastic cartilage.*

Osseous Tissue.—Osseous tissue comprises the osseous framework, the medulla, and the periosteum.

The **framework**, which has everywhere the same composition, is made up of parallel lamellæ and bone corpuscles. In a section of dry bone the **bone corpuscles** appear as ovoid bodies when seen edgewise, but rounder if seen flatwise. From every side of them spring numerous canals which ramify and anastomose with those arising from neighbouring corpuscles. Virchow has shown that these corpuscles correspond to cellular bodies. If a fragment of bone be decalcified by the action of hydrochloric acid and boiled, the masses showing these incomplete ramifications, and which he looked upon as cells, can be isolated. In some of them he was able to perceive nuclei. These nuclei are extremely distinct, and are always present in every osseous corpuscle. They can be perceived in all, if, after having decalcified a bone by chromic or picric acid, fine sections are made and stained with aniline red dissolved in acetic acid, or with an ammoniacal solution of carmine, or better still with a solution of purpurin. The stellate body which Virchow succeeded in isolating by means of hydrochloric acid is not a cell but a species of capsule. The true osseous cell is contained within it. It has the appearance of a protoplasmic mass surrounding a nucleus, and in the adult bone looks flat. The cellular nature of the bone corpuscle is thus perfectly demonstrated. The numerous canaliculi proceeding from it are intended to carry nutritive fluids to different parts of the osseous substance, which does not itself possess the property of imbibition, and very probably is not capable of giving rise

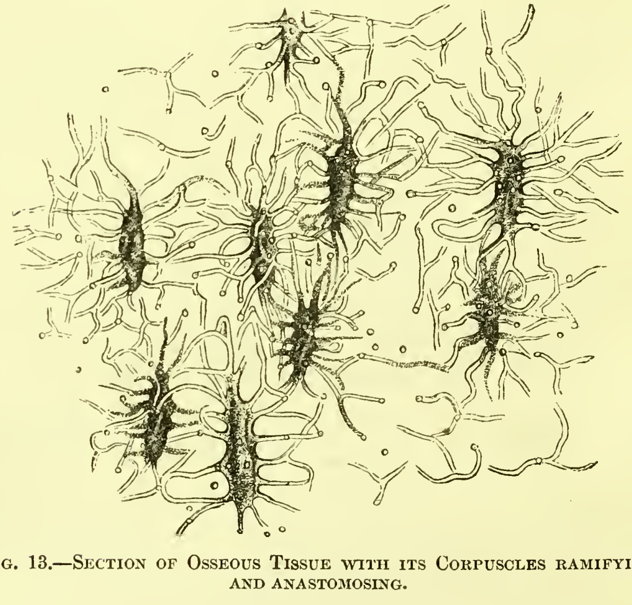

FIG. 13.—SECTION OF OSSEOUS TISSUE WITH ITS CORPUSCLES RAMIFYING AND ANASTOMOSING.

to any of the phenomena of endosmosis necessary to nutritive changes.

Bone corpuscles are situated in the middle of the bony lamellæ, and are parallel to their planes of separation. The osseous lamellæ form systems by their union; it is thus that systems of lamellæ parallel to each other are arranged on the surface of bone, and that every medullary cavity is regularly surrounded by them, in the compact, as well as in the spongy, tissue.

The **medullary cavities** contain the medulla and blood-vessels; in the long bones they are generally cylindrical, and run in a direction parallel to the axis of the bone. These are called the **Haversian canals,** and are united by transverse or oblique canals. The cancellous tissue does not differ from the compact except by the larger size and the less regular form of its canals. The medulla is always traversed by blood-vessels. Between them and the walls of the medullary spaces there are: 1, small round granular cells measuring 10 μ to 15 μ, with a large and well-defined nucleus (the *medullocelles* of Robin); 2, large cells of irregular shape and with many nuclei interspersed in their substance (the *myéloplaxes* of Robin) (fig. 4, a, b); 3, round cells having many nuclei in their centre, or one nucleus folded on itself and throwing off buds (*the cells with budding nucleus* of Bizzozero); 4, adipose cells; 5, connective-tissue cells accompanying the blood-vessels. These different elements exist in varying proportions in different bones, and according to the phase of development of the osseous tissue. In the bones of the limbs, the adipose cells predominate; in the bodies of the vertebræ and in the sternum the non-fatty elements are the most numerous; hence the redness of the medulla. The medulla is the seat of the most important nutritive and pathological phenomena which take place in the bones.

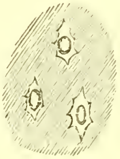

FIG. 14.—BONE CORPUSCLES OBSERVED IN A FRAGMENT OF DECALCIFIED BONE AND STAINED WITH CARMINE.

The **periosteum** is a fibro-elastic membrane analogous to an aponeurosis, a fact which struck Bichat. The periosteum surrounds all parts of the bone, and stops at the commencement of the articular cartilages. It is composed of fibrous and elastic tissue, which in its deepest layer, that which is in contact with the bone, is formed of very fine and close fibrils. The vessels of the periosteum are very numerous, and detach themselves from its deeper layer to penetrate directly into the bony canals. The osteo-periosteal vessels play an important part in pathological subperiosteal phenomena.

The development of osseous tissue is extremely interesting, in that osseous tissue is not formed directly from embryonic cells, but from fibrous and cartilaginous masses which have already taken the form of the bone; and as in pathological conditions transformations of tissue are often observed, that which takes place in bone has served as a basis and objective point for all anatomo-pathologists. They have, in fact, based upon osteogenesis their general comprehension of pathological histogenesis.

The formation of pathological tissue at the expense of healthy tissue differing from it has been called *heteroplasia* by Virchow. The development of osseous tissue from fibrous and cartilaginous tissue is the physiological type of heteroplasia. Virchow did not look upon it from this point of view, for he considered osseous and cartilaginous tissues to be histological equivalents, and that osseous tissue is developed in consequence of nutritive changes in fibrous and cartilaginous tissues, consisting especially in incrustation of the fundamental substance with calcareous salts. Virchow applied what takes place in rachitic bone to the normal development of bone. But on studying more thoroughly the phenomena of normal ossification, Henry Müller constructed an entirely new theory. Continuing these researches, we have ourselves verified the fact that bone always develops according to the same general law, whether from cartilage, or under the periosteum, or from fibrous tissue.

A. **Intra-cartilaginous ossification** takes place in the following manner: the cartilage cells increase by the process we have already described; the new cells are surrounded by secondary capsules (fig. 12, *a*); the mother cells, being full of them, enlarge and become elongated by reciprocal pressure, so as to converge towards the point of ossification. The matrix of the cartilage is split up so as to appear fibrillated; it is soon infiltrated with calcareous salts. At this moment, in consequence of the influence exercised by the blood-vessels, which have spread from the periosteum or from the already formed medullary cavities, the secondary capsules are dissolved and the cartilage cells are set free and proliferate (*a*, *e*, fig. 15); they then take on the characters of embryonic cells described above—at this stage they may show amœboid processes. The cartilaginous tissue is destroyed, but the osseous tissue does not yet exist.

This new tissue, which has not yet received a name, and which we propose to call **ossiform**, consists of trabeculæ incrusted with calcareous salts, and represents the matrix of the old cartilage (fig. 15, *f*). *In these trabeculæ there are no cellular elements.* They are the boundaries of the cavities or alveoli which, communicating with one another, form cavernous spaces (fig. 15, *g*) filled with a vascular medullary tissue. The ossiform tissue in no way

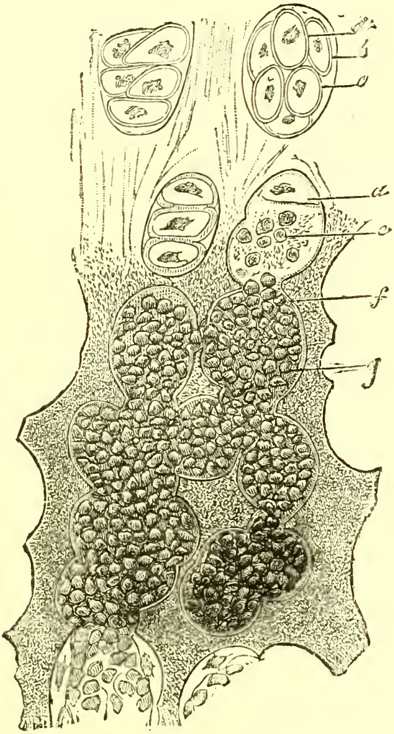

Fig. 15.—Intra-cartilaginous Ossification.

a, primitive capsule filled with secondary capsules; *d*, cartilage cell of which the capsule is about to disappear; *e*, proliferation of cells resulting in the formation of embryonic medullary tissue; *g*, channels filled with new medullary tissue, and bounded by the calcified matrix, *f*. At the lower part of this figure stellate bone corpuscles begin to appear. Magnified 250 diameters.

corresponds to the description of Virchow's osteoid tissue, nor to the spongeoid tissue of Guérin and Broca. These authors based their descriptions on observations of rachitic bone. Now, as we shall see when studying rickets, the usually calcified trabeculæ of the osteoid or spongeoid tissue of these authors contain cellular elements.

In ossiform tissue, vessels from the bone penetrate into the alveoli and form loops. Then begins true ossification. The cells of the embryonic medulla arrange themselves along the calcified trabeculæ; they are often pressed one against the other, and form along the osseous trabeculæ, undergoing development, a continuous layer simulating an epithelium. Gegenbauer has given the name of *osteoblasts* to these cells. Around some of those which have already sent out processes a new intercellular substance is deposited; this is the osseous material. Cells may be seen but half enclosed in the osseous deposit, the rest of their surface—that turned towards the medulla—being free. Soon, however, they are completely surrounded by the bony material, and become veritable bone corpuscles. To this first layer new ones are added, always by the same mode of formation, and at the expense of the medulla. It is thus that a medullary space, primitively irregular, is transformed into a Haversian canal, containing medulla and vessels. After the above description, we do not consider it necessary to enter into more circumstantial details as to the formation of the various bones and the various kinds of osseous tissue.

B. **Sub-periosteal ossification.**—Hitherto we have only considered the formation of bone from primitive cartilage; but, once formed, the bone can continue to grow and to increase in thickness by the deposition of new layers beneath the periosteum. This growth takes place in the following manner. Beneath the periosteum there is, at this period, a layer of round or polygonal cells containing one or more nuclei, differing in no way from cells of embryonic medulla. In the midst of this layer, examined in transverse sections of bone, straight or curved osseous needles advance. Their bases are continuous with the old bone, their free extremities being directed towards the periosteum. The medulla cells pressed against the surface of these needles of bone are then seen to be successively surrounded by osseous substance. Here again cells may be seen half within the osseous and half within the medullary tissue, so that the process of sub-periosteal ossification is identical with that observed in the second phase of ossification from cartilage. These needles, in the centre of which connective tissue fibres are always present, correspond to vertical sections of laminæ; they gradually increase in size, curve over, and unite together, and end by bounding a round space corresponding to a Haversian canal.

The connective-tissue fasciculi, which are found in the centre of the sub-periosteal osseous needles, persist in the bone when completely formed; they occupy a position in the parts intermediate to the Haversian systems. They were first discovered by Sharpey, and they are known under the name of *Sharpey's fibres*.

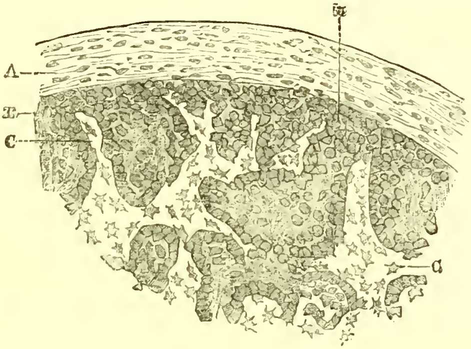

FIG. 16.—SUB-PERIOSTEAL OSSIFICATION.

A, transverse section of the periosteum showing connective-tissue cells; B, medullary tissue; C, osseous trabeculæ containing stellate osseous corpuscles. All along the osseous trabeculæ there is a close layer of medullary cells flattened by reciprocal pressure. Many of these cells may be seen undergoing transformation into bone corpuscles. Magnified 120 diameters.

C. **Intra-membranous ossification.**—In the bones of the skull osseous tissue is developed from a fibrous membrane, and from trabeculæ which gradually increase in thickness, curve over, and limit the medullary spaces. In the human embryo two to three months old, osseous plates are found corresponding to each of the bones of the skull. These bones terminate in the fibrous tissue by needles. Along these needles are seen one or two layers of embryonic cells, polygonal by reciprocal pressure, altogether similar to the osteoblasts observed beneath the periosteum and in the medullary cavities. These cells become bone corpuscles by an analogous process.

The osseous needles terminate in the fibrous tissue by a long filament formed of a refractive and vaguely fibrillar substance containing no cells. These fibres are in every way comparable to the trabeculæ of the matrix of cartilage which we have studied in the first mode of ossification, and constitute Sharpey's fibres in the adult bone. They seem to be the result of a special condensation of certain bundles of connective tissue, and serve to direct the process of ossification.

The embryonic cells which line the osseous trabeculæ are evidently derived from the surrounding connective tissue, the cells of which proliferate.

The same general law is therefore seen to regulate everywhere the formation of osseous tissue, and may be formulated thus:—

The ground substance of the tissue (cartilage-capsules and cells or fibrous substance) is partially dissolved; the cells proliferate, become free, give rise to an embryonic tissue the elements of which are surrounded by a new ground substance, and become bone corpuscles.

This process of bone-formation by a veritable physiological heteroplasia will be found to have numerous applications in pathology.

GROUP II. Muscular and Nervous Tissues.

Muscular tissue.—In man there are three distinct varieties of this tissue to be considered: 1, the muscles of organic life, formed of fusiform cells, which contract slowly and involuntarily; 2, the muscular tissue of the heart, the fasciculi of which are striated, anastomose together, and contract in a brusque and involuntary manner; 3, the muscular tissue of the trunk and limbs, composed of non-anastomosing striated fasciculi, and characterised physiologically by brusque and voluntary contractions.

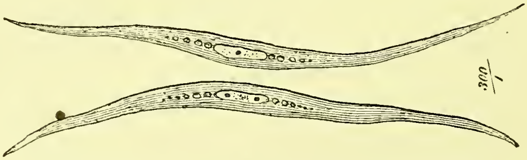

FIG. 17.—ISOLATED SMOOTH MUSCULAR FIBRES.

The elements of the muscles of organic life are fusiform cells varying from 40 μ to 200 μ in length, and in which the existence of a cell wall has never yet been definitely ascertained. They appear to be formed throughout of a transparent refractive and amorphous substance, but which is in reality composed of continuous fibrils. In the centre of the cell there is an elongated rod-shaped nucleus, which becomes apparent after staining with carmine and treating with acetic acid, the latter causing it to assume a serpentine form. The nuclei of the smooth muscular fibres possess one or many nucleoli, described by Frankenhäuser. The nuclei are separated from the contractile material by a granular protoplasmic mass, particularly abundant at each extremity.

The cells of involuntary muscular tissue are rarely found in an isolated state in the midst of the tissues (the middle wall of the large arteries). They are more often united, sometimes to form bundles, sometimes to form membranes as in the arterioles. They are then bound together by a cementing substance, so that it becomes difficult, if not impossible, to separate them. Their complete dissociation may be, however, obtained by means of certain reagents, such as a 20 per cent. solution of nitric acid (Kölliker), or a 40 per cent. solution of potash (Weismann). According to most histologists, Kölliker among others, these muscle-cells are derived directly from embryonic cells, the protoplasm of which, after undergoing successive changes, is transformed into muscular substance, the nucleus elongating and becoming rod-shaped.

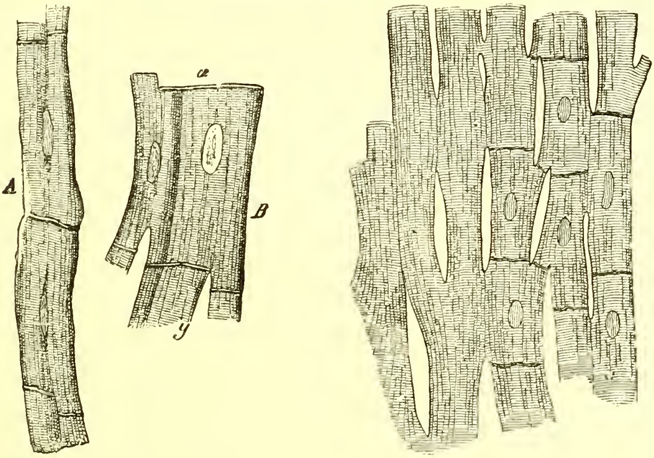

FIG. 18.—MUSCULAR FIBRES OF THE HEART,
separated by transverse lines which indicate the limit of the component cells.

The muscular fasciculi of the heart are also derived from embryonic cells; their ground substance is always striated, and oval nuclei occupy the centre of the bundles. The cells forming part of a cardiac fibre never melt into one another, and even in the cardia of adults their boundaries can be determined. Weismann, by treating fragments of myo-cardium with a 40 per cent. solution of potash, was enabled to isolate the component cells, whilst

Eberth, by means of nitrate of silver, has outlined the limits of each cell in the muscular fibres of the heart (fig. 18).

Voluntary striated muscular fibres are developed from embryonic cells which elongate, the nucleus becomes ovoid and multiplies, the protoplasm also undergoes certain nutritive changes which transform it into striated material, whilst at the same time an amorphous resisting membrane, destined to become the sarcolemma, is developed around the cell. At the commencement of these changes only the peripheral part of the protoplasm undergoes the changes which result in muscular tissue; there always remains around the nuclei, which in the mammiferæ are finally conveyed to the periphery of the muscular substance, a certain amount of unchanged protoplasm. The nuclei are found under the sarcolemma surrounded by a small fusiform mass of protoplasm. This protoplasmic substance extends, moreover, in the form of extremely fine laminæ throughout the thickness of the fasciculus, dividing it into longitudinal columns (*primitive cylinders* of Leydig); these columns are again separated by protoplasm into cylinders of a diameter scarcely exceeding 1 μ (*primitive fibrillæ*).

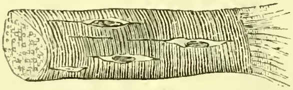

Fig. 19.—Striated Muscular Fibres.

Such is the origin of the longitudinal striation of muscular fibre. The transverse striation, which is so distinct as to strike the observer at once, and which has given muscular bundles the name of striated fibres, must be looked upon as a kind of geometric arrangement of the contractile parts of muscular substance. These, to which Bowman was the first to draw attention, have been described under the name of **sarcous elements.** According to Bowman, the contractile substance is essentially composed of little prisms placed regularly end to end one against the other and bound together by a cement. This view of the composition of striated muscular fibres is corroborated by the action of certain reagents, of which some (alcohol, chromic acid, bichromate) favour the longitudinal division of the primitive fasciculus into fibrils, whilst others (gastric juice, dilute organic acids, caustic alkalies) cause the separation of the same fasciculus into discs superposed like coins in a pile of money.

According to Bowman's theory, there are in the muscular fibre neither longitudinal fibrils nor transverse discs, but sarcous elements united by a longitudinal cement soluble in alcohol, chromic acid, &c., and by a transverse cement soluble in gastric juice, the dilute organic acids, and caustic alkalies. This view of Bowman's has held sway for ten years, though it ought to have been destroyed by the observations, no longer recent, of Amici,—observations which have been confirmed and extended by Krause, Hensen, and ourselves. In the transverse lines which separate the sarcous elements a fine striation is present which has the same optical characters as the sarcous elements themselves. The sarcous elements are, moreover, divided transversely into two equal parts by a clear line.

It results from these observations that the structure of the striated fasciculi is not so simple as Bowman supposed, in fact, they have a very complex structure. If we examine an isolated fibril, which can be easily obtained by dissociating the muscles of insects' wings, we see after staining with picrocarminate of ammonia or with hæmatoxylin that there are in successive order: 1, a thick disc, divided into two equal parts by a clear stria; 2, a clear space; 3, a thin disc; 4, another clear space; then a thick disc and so on.

This arrangement, which is that of all striated muscles, is related to their mode of contracting, in which two factors come into play: 1, contractility appertaining to the thick discs; 2, elasticity, which seems to depend on the thin discs and the intermediate portions between the thin and thick discs.

Nervous tissue.—The elements of nervous tissue are cells and fibres.

Nerve-cells are very variable in form and in size; they vary between 10 μ and 100 μ; they are always furnished with simple or branching processes, which connect them with one another and with nerve-fibres. Among these processes there is one, discovered by Deiters and bearing his name, which arises from every motor nerve-cell of the spinal cord and of the brain. It is homogeneous, vitreous, does not branch, and is evidently the origin of the axis-cylinder process of the medullated nerve-fibre. It is therefore called by the name of the axis-cylinder process (*a*, fig. 20). Nerve-cells of the centres have manifestly no cell wall; their fundamental substance is finely granular, often containing pigment granules, and is striated towards the periphery. All nerve-cells have a nucleus showing a double contour and containing one or

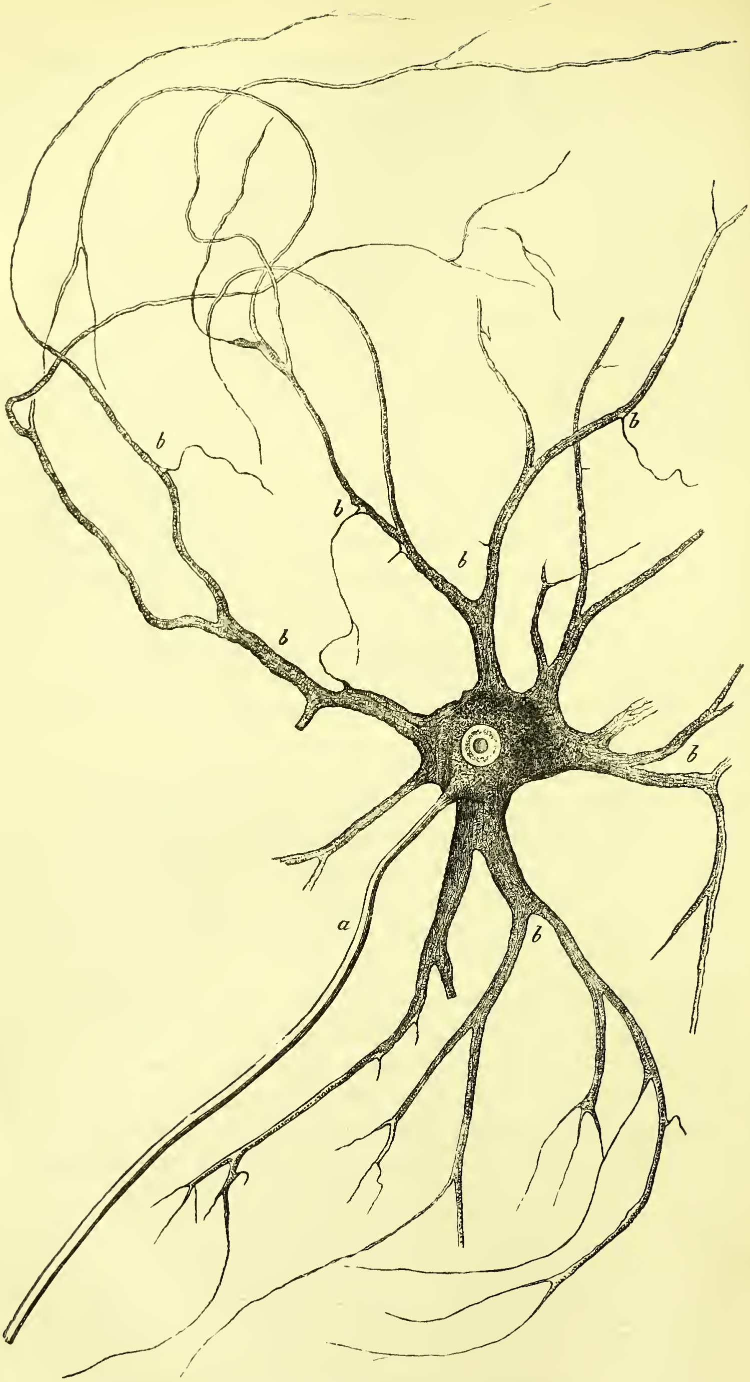

FIG. 20.—MULTIPOLAR NERVE-CELL FROM THE ANTERIOR HORNS OF THE SPINAL CORD OF THE OX. After Deiters.

a, axis-cylinder process; *b*, *b*, processes, called protoplasmic. Magnified 300 diameters.

two nucleoli. Such are the cells of the grey matter of the brain, of the cerebellum, and of the spinal cord. In all the spinal ganglia the nerve-cells are round. They have only one process; they are enclosed in a delicate capsule composed of a supple, homogeneous, and elastic substance; the inner surface of this capsule is lined with endothelial cells.

According to Remak, Kölliker, and Lockhart Clarke, nerve-cells are developed from primitive embryonic cells.

Nerve-tubes or fibres are of two kinds; those having a sheath of myelin (medullated nerve-fibres or dark-bordered fibres), and those having no medullary sheath. In the embryo the latter only exist. In the course of development the medullary sheath is added.

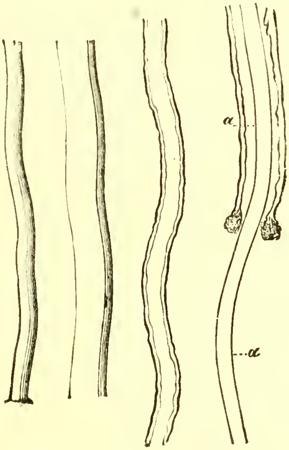

FIG. 21.—NERVE-FIBRES.

a, a, axis-cylinder partly surrounded by the medullary sheath.

Medullated nerve-fibres may be divided into two classes—those of the peripheral nerves, and those of the nervous centres. The former are limited by a resisting structureless membrane, called the **membrane of Schwann.** At regular distances the fibres are constricted, and appear as if they had been included in a ligature (*a*, fig. 22), hence segments of equal length (inter-annular segments) are formed. These segments vary in length with their diameter; in the largest they are more than a millimetre. The myelin is not continuous from one segment to another; there is a solution of continuity at each constriction. The membrane of Schwann appears as if it passed over all the segments of the same nerve-fibre, but actually it is composed of as many fragments as there are segments, for nitrate of silver reveals a line of junction always situated where the break occurs.[1] Every medullary tube is traversed in the direction of its axis by a cylinder, homogeneous and vitreous in appearance, and of which the diameter is in accordance with that of the medullary sheath. This cylinder (the axis-cylinder, axial fibre, primitive riband) is continuous—that is to say, it passes through the medullary tube from its origin to its termination without undergoing any interruption or junction at the annular constrictions. Near the centre of an inter-annular segment a flattened oval nucleus is perceived, under the membrane of Schwann, and lodged in a depression of the myelin. It is surrounded by a granular protoplasmic layer,

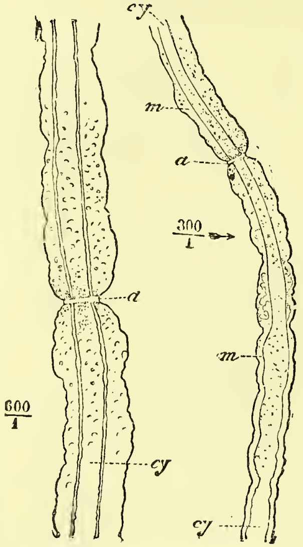

FIG. 22.—NERVE-TUBES SHOWING ANNULAR CONSTRICTIONS.

a, annular constrictions; *cy*, axis-cylinder; *m*, myelin.
Magnified 300 to 600 diameters.

which, extending beneath the membrane of Schwann, lines it in its entire extent from one constriction to the other. At the constriction this layer folds on itself and is reflected on to the axis-cylinder, constituting a special sheath to it—a sheath of which Mauthner long ago observed the existence without recognising its significance. We have, however, designated it the *sheath of Mauthner*. The result of this arrangement is that the myelin of each inter-annular segment is contained within a protoplasmic sac, formed of an extremely fine layer, and containing one

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[1] These constrictions are known as the *Nodes of Ranvier*.—TR.

nucleus. Between the protoplasmic layer which envelops the axis-cylinder, and that which lines the sheath of Schwann, there are extremely fine oblique partitions, dividing the myelin into a series of short segments nested one within the other. After the action of certain reagents they appear as if separated by indentations, which were lately described by Schmidt, Lantermann, Franz Boll, &c.

Myelin is formed of a fluid oleaginous material which, if not retained by the membrane of Schwann, would easily escape, and also probably accumulate in the most dependent parts if not supported by numerous partitions. On dissociating a fragment of a nerve in water the myelin is seen to escape at the points where the tube is broken or where the membrane of Schwann is torn. It escapes in the form of beaded filaments, which soon join together, swell, and change into more or less circular spherules of variable size. Their edges are well defined, and they have a double contour. This is one of the most important characters of myelin. Osmic acid stains it a blue-black, whether contained within the nerve-fibre or free. The same reagent stains fat of a more or less pronounced brown tint.

The **axis-cylinder** is stained with carmine; and though it usually appears homogeneous and vitreous, it seems under certain circumstances to be composed of a bundle of fine and delicate fibrils. When a nerve-fibre divides near its peripheral extremity, the division always occurs at an annular constriction. The axis-cylinder divides itself between two new nerve-fibres, as if the bundle of fibrils which composed it had been simply separated into two. A new division conducts in two different directions the nerve-fibrils which hitherto had travelled together from their origin in the nerve-centres. If the axis-cylinder have really a fibrillar composition, as certain observations might lead us to suppose, we must remember, with Waldeyer, Schultze, and a number of other observers, that physiologically the essential element of the nerve is the nerve-fibril. It is on this that the function devolves of bringing a given limited part of the centres into relation with an elementary peripheral organ, sensory or motor.

In the nervous centres (brain and spinal cord) the medullated nerve-fibres have no sheath of Schwann, and consequently no annular constrictions or inter-annular segments. The myelin of these fibres seems to be limited externally by a soft protoplasmic envelope which is easily torn; when torn, the myelin escapes in droplets, or distends the sheath in such a way that the fibre becomes varicose. Medullated fibres of small diameter present similar changes when isolated by simple dissociation, or when submitted to the action of certain reagents.

Non-medullated fibres bear also the name of Remak, who discovered them. They are found mixed in variable proportion with the medullated fibres in all peripheral nerve-trunks. They are abundant in the sympathetic and pneumogastric nerves. They anastomose with one another so as to form a closely woven network. In other words, fasciculi of the fibres of Remak are found in the nerves, and in these fasciculi the fibres anastomose. Different fasciculi of the same nerve also send out anastomotic branches. The fibres forming this close network are of variable diameter. They are generally cylindrical but sometimes flattened. They are distinctly striated longitudinally, and appear to be composed of fibrillæ steeped in a binding protoplasmic substance, which forms a continuous layer at the surface of the fibre. On this protoplasmic surface of the fibres of Remak, flattened oval nuclei are always found, causing a more or less marked external projection. They are not present at equal distances.

At their peripheral termination the medullated fibres often lose the sheath of myelin and become pale fibres; but they differ from the fibres of Remak in that they do not anastomose. Exception must be made for certain plexuses, into whose composition nerve and ganglionic cells enter.

Nerve-fibres of whatever kind are processes of nerve-cells, their axis-cylinder proceeding from some one of the processes of these cells. The peripheral endings of nerve-fibres are only known in a certain number of organs and tissues; they constitute special organs; of such are the corpuscles of Pacini, Meissner, and Krause, and the nerve-endings of the voluntary striated muscles. We do not know their pathological lesions, and are therefore dispensed from dwelling on them.

GROUP III. **Epithelial Tissues.**

Epithelial cells are of very different forms and sizes; they may be polygonal, very much flattened (laminated), equal in their different dimensions (cubic), or elongated in the shape of a cone or cylinder, while some present peculiarities by which they may be recognised as epithelial cells when isolated. Such are the dentate cells of the middle layer of the *rete mucosum*, as also the ciliated cells, cylindrical in the air and genital passages, and polygonal in the cerebral ventricles; so also the striated, platter-like cells of the intestine, and the cylindrical cells with terminal ramifications of the organs of sense. Similarly the cells filled with mucus of the mucous glands, as well as the chalice cells so abundant in the broncho-tracheal, digestive, and genito-urinary mucous membranes, together with the cells of the cornea and the fibres of the crystalline lens, can easily be recognised.

An epithelial cell, however, only assumes its characteristic form subsequent to evolution. Evolution is the capital physiological characteristic of epithelial tissues. All their elements are transitory; they are created, develop, and die in a varying space of time. Thus in the skin in the deepest layer of the *rete mucosum* in contact with the papillæ, cylindrical dentate cells are found, which soon tend to become spherical, while still preserving their dentate border, and slowly increase in size as they pass from the deeper layers to the surface of the epidermis; they finally become flattened into dried laminæ, and form by their union the horny layer, from which they are thrown off by physical and chemical agencies. In buccal epithelium the same evolution is seen except the stage of horny transformation. So also in the mucous membrane of the trachea, the deep cells are oval, and only the superficial acquire a larger diameter, take the true cylindrical form, and become ciliated at their surface.

Though isolated epithelial cells do not always possess characters by which they may be recognised, we have in the structure of the epithelial tissue itself elements for the exact definition of the tissue. The cells which compose it are united with one another so as to form masses or membranes, modelled exactly on the surfaces to which they adhere. Further, blood-vessels are never observed in epithelial tissue.

The epithelial coverings originate thus: the epidermis and the cutaneous glands from the external layer of the blastoderm; the epithelium, the mucous membranes, and their glands from the internal or mucous layer of the blastoderm; the other epithelial coverings, those of the blood-vessels and serous membranes, are, on the contrary, derived from the middle layer of the blastoderm. This embryogenic difference has led His, Thiersch, and Rindfleisch to establish well-marked divisions, from the physiological and pathological points of view, according as the epithelial tissues originate from the cutaneous, mucous, or middle layers. His thought it necessary to give them different names, so he called the two first epithelial, the last endothelial. He believes that this difference of origin always corresponds to a difference in structure, endothelium being composed of very flat cells united by their edges and forming a single layer (endothelium of blood-vessels, serous membranes, articular synovial membranes, serous and mucous bursæ), epithelium having on the contrary one or more layers of thicker cells. But even from this point of view there is a great resemblance between the two kinds of epithelium. Thus, that lining the pulmonary alveoli, and which is derived from the mucous layer, is very thin, and resembles that of the serous membranes, whilst the epithelium of the synovial fringes, derived from the middle layer, is formed of globular cells sometimes arranged in superimposed layers; moreover, it secretes a fluid charged with mucin similar to that of the mucous membranes. Again, the flattened form of the cells of the endothelial tissues of His seems to us to be related to mechanical causes, and may be explained in blood-vessels by the pressure and friction of the blood, and in serous membranes by the pressure and friction of opposed surfaces.

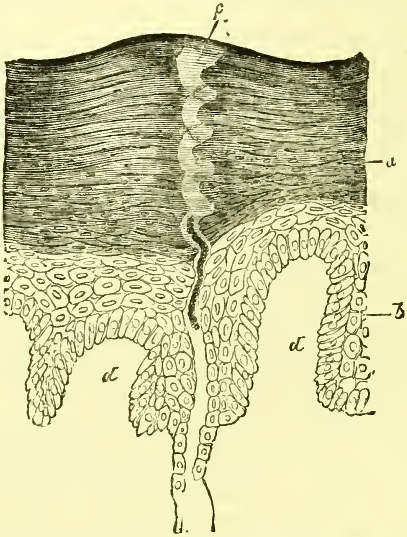

FIG. 23.—SECTION OF THE VARIOUS LAYERS OF THE EPIDERMIS.

The papillæ, *d*, are covered by cells which are first cylindrical, then scaly, *b*, forming the mucous layer of Malpighi. In the superficial layers, *a*, the cells are flattened and laminated; *c*, the channel of a sudoriparous gland; *d*, papillæ of the derm. (Figure borrowed from Leydig.)

It will be seen when treating of pathology that purely physical conditions may modify the form of epithelial cells. The distinction made by His is not therefore absolute; moreover, it is based on embryogenic facts which are far from being well established, for example, on the derivation of the Wolffian body and the ovary from the external layer of the blastoderm.

Epithelial tissue is divided into investing, and glandular, epithelium.

Investing epithelium.—Investing epithelium is formed either of stratified layers, or of a single layer of cells.

Of *stratified epithelium* two varieties may be distinguished —1. That in which the superficial cells are flat, this is seen in the skin, the buccal mucous membrane, the pharynx, œsophagus, conjunctiva, bladder, urethra, vagina, &c.; in the skin the superficial cells form the horny layer, the nails, and the hairs according to the disposition of the parts. 2. That in which the superficial cells are cylindrical and ciliated, as in the respiratory mucous membrane from the nasal fossæ to the ultimate bronchi, with the exception of the vocal cords.

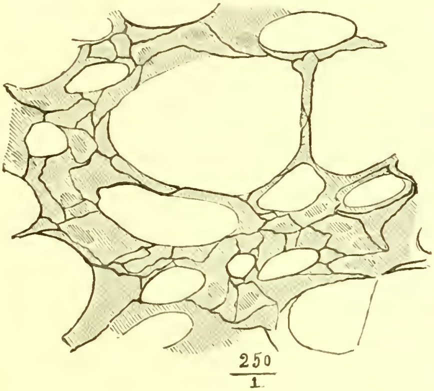

FIG. 24.—TRABECULÆ OF THE GREAT OMENTUM OF THE RAT

Covered by a pavement epithelium, the intercellular lines of which are brought out by nitrate of silver staining.

Epithelium composed of a single layer of cells is either cylindrical or tessellated.

It is *cylindrical* in the digestive mucous membrane, cylindrical and ciliated in the uterine mucous membrane, in the Fallopian tubes, the vasa deferentia, and the seminal vesicles. In the mucous membrane of the small intestine the cells bear a striated border.

Tessellated epithelium composed of a single layer of cells is met with in the cerebral ventricles, the pulmonary alveoli, the arachnoid, pleura, peritoneum, pericardium, and the blood-vessels. Pavement epithelium cells are sometimes cuboid, as in the ventricles of the brain, sometimes flat and laminated, as in all the other organs cited. In the latter case a good idea of epithelial investment can only be obtained by staining with nitrate of silver. In well-made preparations the intercellular cement appears in the form of black sinuous lines bounding extremely fine cells (fig. 24). When a tissue thus stained with nitrate of silver is coloured with picrocarminate of ammonia, and afterwards submitted to the action of oxalic acid, the nuclei appear beneath the laminæ, while in some cases a distinct mass of protoplasm can be seen around them. The nucleus and the protoplasm only occupy

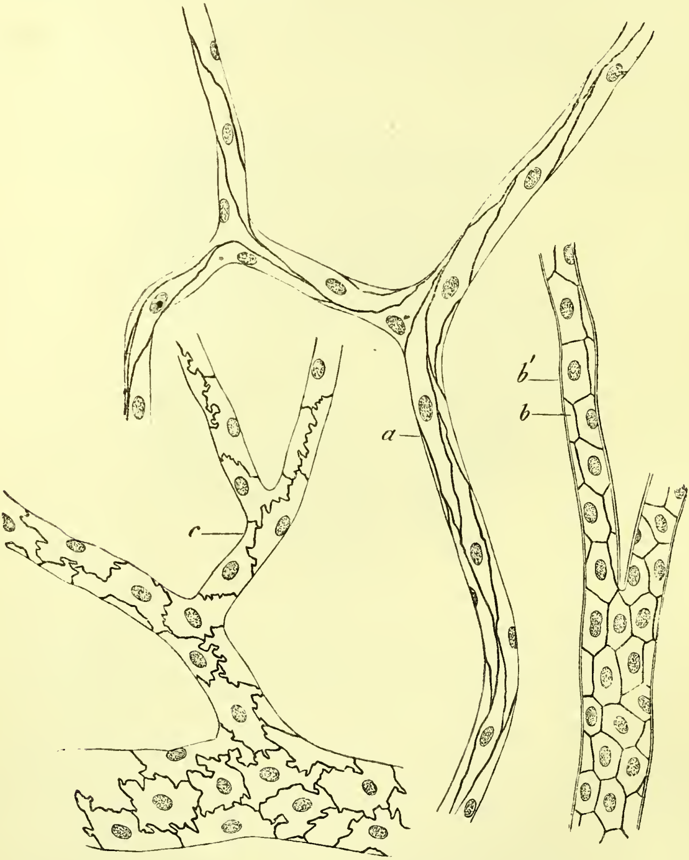

Fig. 25.—Capillary Vessels in Various Animals.

The borders of the endothelial cells are stained with nitrate of silver. (Figure borrowed from Eberth.)

a portion of the plate and are moulded into the subjacent connective tissue. The plate seems to be the result of a secondary exudation of the active cell. We will return to this subject when considering inflammation, studied in epithelial tissues.

The internal surface of all the blood-vessels is lined throughout with such an epithelium. Formerly it was believed that the capillaries were formed of an amorphous membrane containing nuclei. Hoyer, Auerbach, Eberth, and Aeby, profiting by Recklinghausen's process by which delicate epithelia may be demonstrated, have succeeded in showing that the membrane of the capillaries is in reality formed of epithelial cells, each one having its own nucleus.

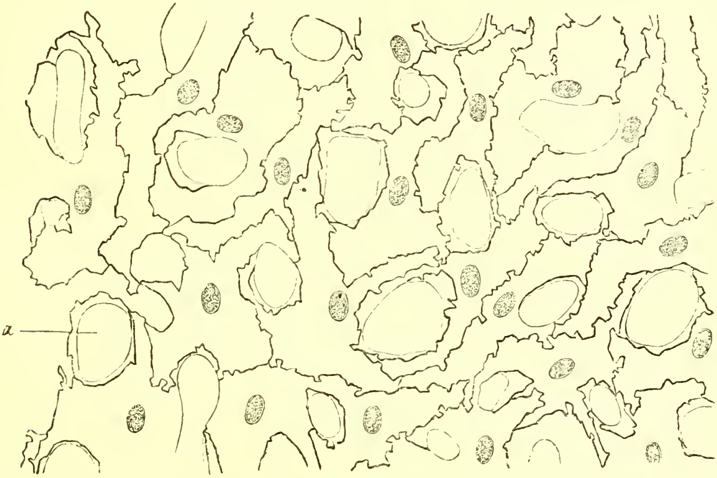

Fig. 26.—Capillary Vessels of the Lung of a Frog stained with Nitrate of Silver.

(Figure borrowed from Eberth.)

The flat form of these cells and their intimate union may prevent their being distinguished by the ordinary methods. But when irritated by inflammation they become turgid and separate from one another.

The epithelium of the capillaries is continuous with that of the arteries and veins, without any line of demarcation. We will return to these vessels when we have to speak of their pathological changes. Before an epithelium had been recognised in the vascular capillaries, Recklinghausen and His had already demonstrated that the capillary lymph-vessels were lined by an epithelium composed of flat cells.

Von Recklinghausen ascertained that solid particles passed easily from serous cavities into lymph-vessels. He observed this fact directly in the peritoneal surface of the phrenic centre of the rabbit.

Later Ludwig and Schweigger-Seidel, while studying the epithelium covering this surface, by the aid of nitrate of silver staining, discovered the existence of stomata between the epithelial cells—that is to say, extremely small openings which seem to establish a communication between the peritoneal cavity and the lymphatic vessels contained in the intertendinous slits. In reality there are large openings between the lymphatics and the surface of the peritoneum, but they are generally obstructed by small cells which are movable on one another, and which may be easily detached, leaving a communication open to the lymph contained in the peritoneal cavity (lymphatic wells). The lymphatics contained in the intertendinous slits, and those which ramify on the pleural surface of the diaphragm, as well as the lymph-capillaries of other organs, have a simple structure resembling that of the vascular capillaries. The endothelium which lines their internal surface is composed of cells of a peculiar shape. At their borders are blunt teeth, which cog with those of adjoining cells. The larger lymphatic trunks have a much more complex structure, resembling that of veins of the same calibre.

Glandular epithelium.—Glandular epithelium lines the internal surface of the ducts and the terminal extremities of glands.

It is in the interior of the epithelial cells which line the glandular *culs-de-sac* that the secretion special to each kind of gland is elaborated. Thus the epithelial cells of the mucous membrane contain mucus; the cells of the pancreas contain all the elements of the pancreatic juice; the cells of the glands of the stomach contain pepsin, &c. To set the cellular secretion free it is not necessary, as Kölliker and Heidenhain erroneously maintained, that the glandular cells should be destroyed. In fact, if we consider the simplest glands, the unicellular mucous glands, the chalice cells which are found scattered in the midst of other cylindrical cells in the intestinal villi, on the bronchial mucous membrane, or on the rugæ of the stomach, it seems evident to us that cells which open more or less on to surfaces pour out the fluid they contain in proportion to the rate and quantity of its elaboration. Analogous phenomena occur during the secretion of the more complex mucous glands, on which experiments have been performed, for example, the submaxillary gland of the dog, where, owing to an irritation of the chorda tympani, an abundant secretion has been induced for some hours, the acini, instead of being filled with transparent mucous cells, containing small granular cells; these are nothing else, as may be ascertained by examining all the intermediate forms between them and mucous cells, than the nucleus and protoplasm of the latter hypertrophied in consequence of the secretory irritation to which they have been subjected.

Glands may be divided in respect to their general form into: 1. *Tubular*—that is to say, composed of a simple tube, the secretory portion of the gland being directly continuous with the excretory duct. They are either rectilinear and lined with a cylindrical epithelium (glands of Lieberkühn, mucous glands of the stomach, of the fundus of the uterus, &c.), or they are coiled up and lined with a pavement epithelium (sudoriparous glands, kidney, &c.). 2. *Acinous*—that is, composed of *culs-de-sac*, more or less numerous, opening into a common excretory duct. The *culs-de-sac* and the excretory duct are either lined by pavement epithelium, as in the sebaceous glands and the mamma, or the *culs-de-sac* are lined by pyramidal epithelial cells and the ducts by a single layer of cylindrical cells, as in the salivary glands, the glands of Brunner, the tracheal and laryngeal glands, and the pancreas.

We will return, in the pathological section, to the structure of the liver and the lymphoid organs. The latter, though an effort has been made to ally them with glands, differ from them in so many points that a separate place must be reserved for them.

III.—Lymph, Blood, Plasma.

The lymph and blood are not, properly speaking, tissues, although they are often considered as such. They constitute with plasma the internal media in which the elements of organs exist.

The blood, driven by the heart into the capillary vessels, lets a part of its plasma escape through the walls of these vessels, according as the blood-tension is more or less considerable. The formed elements which the blood contains can under certain conditions, and even in the physiological state, pass through the vascular walls and be diffused with the plasma in the meshes of the neighbouring tissues. These meshes, which are most frequently part of the connective-tissue system, hence receive a plasma rich in nutritive material and charged with oxygen.

From the plasma, which bathes the essential elements of the organism, they draw the materials necessary for their nutrition and function, and discharge their waste into it. Hence it is necessary for the plasma to be incessantly renewed ; it is therefore carried away by the lymphatics whilst a fresh supply constantly arrives by transudation through the walls of the blood-vessels. To understand this process, the circulation of fluids in a large serous cavity—the peritoneum, for example—should be considered. It is known that, physiologically, this cavity contains a fluid which lubricates its surface as well as that of the organs contained within it. This fluid is plasma furnished by the blood, and transuded through the walls of the capillaries and the serous layer covering them. It is rich in albumen, contains some fibrin, together with lymph-cells and a few red blood-corpuscles. Between the serous cavity and the lymphatic system large communications exist (see p. 40), so that in the peritoneum there is a circulation of plasma, which, though very slow, still allows of the interchange of materials necessary for the life of histological elements ; the serous cavities may therefore be looked upon as adjuncts of the lymphatic system.

The connective tissue of the organs present networks enclosing special tissue elements (muscular fasciculi, nerve-fibres, glands, &c.). These networks, which are the analogues of serous cavities, receive plasma and return it to the lymphatic vessels with which they are in communication. In this vast plasmatic system, comprehending the sanguineous, lymphatic, and connective-tissue systems, the blood, the lymph, and the plasma properly so called have to be separately considered.

The blood.—The morphological elements of the blood in the normal state are the red and white corpuscles ; by the aid of the microscope, elementary granules floating in the serum may also be recognised, and, when coagulation has taken place, a reticulum of fibrin. Crystals are spontaneously formed, or may be produced by very simple methods.

To study microscopically normal or pathological human blood, a drop is drawn by means of a prick of a needle at the end of the finger, round the base of which a ligature has been placed. The glass slide on which the blood is placed should be absolutely level. To compensate for dessication, which takes place very quickly at the edges of the drop, the slide should be breathed upon till a slight dew is deposited. It is then covered by a thin cover-glass, and the blood is spread out in an uniform manner between the two glass surfaces, care being taken that the drop in spreading out does not entirely fill all the capillary space contained between the slide and the cover-glass. In a preparation thus obtained, the red corpuscles, if the examination is made rapidly, are seen to be separated from one another in a regular manner, or to form ill-defined groups; soon however they run together, their surfaces are applied one against the other, and they adhere in series which have been compared to rouleaux of money. Between these rouleaux of red corpuscles are found serum, elementary granules, and white corpuscles.

The **red corpuscles** of human blood are discs slightly depressed in the centre; when seen edgewise, they have the form of a bi-concave meniscus. Seen flatwise, they appear either to have the centre dark and the edge light, or the edge dark and the centre light, according to the focal position of the lens. When the lens is moved away from the focal point, the centre is dark, when it is within the focal point, the centre is light. We give these details so that the depressed centre of the red corpuscles may not be mistaken for a nucleus, which may happen to beginners. The red corpuscles seem less strongly coloured in proportion to the magnifying power with which they are examined; thus with a lens magnifying 800 diameters they appear of an extremely pale yellow tint; seen edgewise, they look deeper coloured than seen flat. The diameter of the red corpuscles is not constant, but varies in a very slight degree. The mean diameter is 7 μ. Side by side with the red discoid corpuscles, red spherical corpuscles may be found with a diameter of only 5 μ and of a darker tint, this is owing entirely to their shape. At the edge of the blood-spot on the slide, at the points where contact with the air causes dessication, notches, the extent and number of which are variable, appear at the edges of the red blood-corpuscles, these increase as dessication progresses. When this change is much advanced, the blood-corpuscles having become spherical look crenated or covered with thorns; blood-corpuscles are often found in this form in the cadaver. When dessication of the blood is complete, the red corpuscles melt away into a mass which splits up. If the red blood-corpuscles are acted upon by water, the water becomes coloured by extracting the colouring matter from the corpuscles. Their diameter is then only 5 μ, and they are so transparent that in order to see them at all the field of the microscope must be very much shaded, or an iodised solution of iodine added.

The colouring matter of the red corpuscles is called **hæmoglobin**; it is soluble in a great quantity of water without decomposing. In very feeble solutions its presence can only be ascertained by the aid of the spectroscope ; but in concentrated solutions it crystallises and gives characteristic crystals. Crystals of hæmoglobin may be obtained by several methods, the object of all being to destroy the red corpuscles and to set free the hæmoglobin without the necessity of adding water. The simplest and the surest of these methods consists of pouring ether, drop by drop, into a bottle containing defibrinated blood, and shaking them together till the blood has lost its bright and opaque colour, and has become transparent as syrup ; this change indicates that the hæmoglobin is separated from the corpuscles and dissolved in the serum. The solution is then left quiet for some hours, and at the end of that time the hæmoglobin will have crystallised out. The crystals of hæmoglobin are of a beautiful red colour when seen in the mass; they have not the same form in different kinds of animals ; in man they are rhomboidal plates. If a solution of hæmoglobin be treated by acids or by alkalies it becomes brown, and a new substance is formed, known under the name of *hæmatin.* Hæmatin does not crystallise, but is precipitated in the form of blackish granules. It combines with hydrochloric acid to form a characteristic crystalline salt, which was known formerly under the name of *hæmin*, but which is a *hydrochlorate of hæmatin.* Crystals of hydrochlorate of hæmatin are produced when fresh or dried blood is acted upon by acetic acid or by a mixture of common salt and acetic acid. Crystals of hydrochlorate of hæmatin are brown rhomboidal plates, and of a very dark colour even when examined with a high power ; they are elastic, and may be folded in the shape of a tile ; they cannot be confounded with any other body, hence to the medical jurist they are a very precious means of recognising blood-stains. To obtain them from a dried blood-stain—on linen, for example—the material must be steeped in water, to which a small quantity of common salt should be added, then acetic acid, and heated to boiling-point. While cooling, crystals of hydrochlorate of hæmatin are produced, and may be easily recognised with a power of 300 diameters. Hæmatin is of importance, pathologically, as it is formed from the blood when effused into the tissues. In this case it is slow in formation. The varying colour of ecchymoses is owing to the gradual transformation of hæmoglobin into hæmatin ; this transformation takes place much more rapidly if the blood is in the digestive tract, particularly in the stomach. Here, acted upon by the gastric juice, hæmoglobin is rapidly converted into hæmatin ; this is the cause of black or melanotic vomit, and of the brown colour of gastric ecchymoses. If the blood remains long in the tissues, another substance besides hæmatin is found, which has not yet been produced artificially, and the composition of which is not known; it is called by the name of *hœmatoidin*, and appears in the form of granules or rhombohedrals of a beautiful orange red, so intense that the colour is strong even with high powers. The most beautiful specimens of these crystals are met with in encysted hæmorrhagic foci, especially those of the brain.

The **white corpuscles**, examined according to the method described above, appear as bodies of a spherical or irregular shape; they have a granular appearance, which gives them a grey tint under the microscope, while some of them even contain a variable number of fat granules. If examined at a temperature above 68°, processes appear on their borders; these are of different shapes, but are never as long as those observed at the normal temperature of the body, between 95° and 100°. In frogs and other cold-blooded animals amœboid processes are seen at the temperature of the surrounding media. They are perceived only in a slight degree when the blood is first drawn from the vessels, and subjected to examination; but they become more and more apparent as the observation is continued. They change shape, give origin to secondary processes, retract and form pseudopodes, by the aid of which white corpuscles make an extremely slow, crawling movement of progression, a movement which it is, however, often impossible to recognise except with the closest attention (see p. 4). The white corpuscles have also the property of seizing upon the corpuscles around them and drawing them into their own substance. This phenomenon may be directly observed under the microscope by mixing a drop of frog's blood with granular carmine or vermilion, &c. The absorption of solid particles by the white corpuscles may take place within the organism.

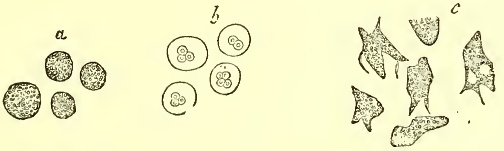

FIG. 27.—PUS CORPUSCLES.

a, as seen in a neutral fluid; *b*, as seen after the action of water or acetic acid; *c*, living corpuscles showing amœboid movements.

To observe this, finely ground vermilion is injected into the vascular system of a frog or warm-blooded animal; aniline blue precipitated by water from an alcoholic solution, or any other solid coloured matter in granules no larger than 5 μ may be used. The blood of the animal is examined a few minutes after the injection. The white corpuscles are found to have already absorbed some of the granules of the injected material. An hour later the white corpuscles have the same appearances, and moreover no coloured granules are found free in the plasma. The red corpuscles never absorb coloured granules. This property which the white corpuscles possess, of moving and of absorbing solid particles when removed from the organism, shows that they are still alive, even though the conditions of their existence seem changed. These vital manifestations of the white corpuscles may be prolonged for a long period if the blood be kept free from germs and in a proper medium, as Recklinghausen has done. We have repeated the experiment of Recklinghausen, placing ourselves under exactly the same conditions. At the end of twenty-two days the white blood-corpuscles of the frog still showed their various properties. This experiment has not been done on the blood of warm-blooded animals, for with them the white corpuscles cease to exist unless the blood is kept at a certain temperature, which is very difficult to accomplish while fulfilling all the conditions of the experiment.

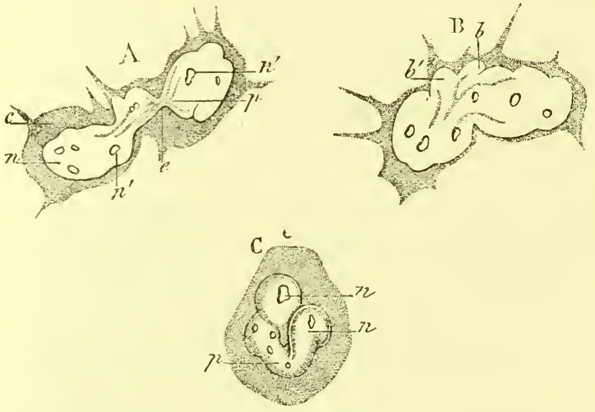

Fig. 28—A, B, Lymphatic Cell of the Blood of the Axolotl examined in the Living State.

A, cell at the commencement of the observation ; *c*, protoplasm with its amœboid processes ; *n*, nucleus constricted at *e* ; *n'*, nucleoli. B, the same cell observed at the end of twenty minutes. The centre of the nucleus is swollen and has two buds, *b*, *b'*. C, white corpuscle of the axolotl treated with a 33 per cent. solution of alcohol ; *p*, nucleus with its buds, *n*, *n'*.

The white corpuscles are much less numerous than the red. In a man in good health one white corpuscle may be counted to three or four hundred red corpuscles. The numeration is difficult ;

therefore to arrive at a correct knowledge of the physiological proportion of white corpuscles to red, and particularly to study their varying proportions—often an useful clinical proceeding—it is well to have recourse to a rapid method. This consists in counting the number of white corpuscles contained in the field of the microscope with a given lens and eyepiece. With eyepiece 1 and lens 6 of Verick, or with eyepiece 2 and lens 7 of Hartnack, or with eyepiece 1 and lens 3 of Nachet, a mean of three white corpuscles will be seen in the field of the microscope in a preparation made as described above. The white corpuscles may be easily isolated from the red corpuscles ; to do this it is only necessary to put a drop of water on one of the edges of the cover-glass ; the fluid penetrates by capillarity, carries the red corpuscles away without moving the white, which remain fixed to the glass surface, by reason of the property which they possess of adhering to the surface of the glass as they adhere to the walls of living blood-vessels in the normal circulation of the blood. After the action of water the white corpuscles show new characters. Under its influence they become spherical and transparent, and in their interior one or more nuclei appear.

Fibrin does not exist already formed in the blood, as was thought before the researches of Denis. The view that Denis held has been taken up and altered during the last few years by A. Schmidt. Schmidt's theory is that which is adopted at the present time in science, although it is still but a simple hypothesis. This author considers that besides albumen there exist in the blood two other albuminoid substances, *fibrinogen* and *fibrinoplastin*, and that a very small quantity of fibrinoplastin is sufficient to change a large mass of fibrinogen into fibrin. Fibrinoplastin is present in the red blood-corpuscles, fibrinogen is found in the plasma. Schmidt, Kühne, and other authors have described methods for extracting these substances from the blood, but they do not say if fibrin is produced by mixing them together. What is absolutely known is that red corpuscles added to certain fluid exudations, that of pleurisy for example, cause the formation of fibrin.

In blood-letting, if the blood is received in a vessel, it coagulates in a mass in a few moments. The clot is at first of exactly the same size as the blood collected, without any change in its appearance, so that coagulation is not perceived except on moving the vessel containing the blood. But at the end of a few hours the clot retracts, condenses, and throws out around it a certain amount of citron-coloured or pinkish serum; the clot may then be said to have lost part of its water of coagulation. When the formation of the clot is slow, as is normally the case in the horse, and in many inflammatory conditions, the red corpuscles, whose density is greater than that of the other constituents of the blood, fall to the bottom of the vessel, the superficial part of the coagulum remaining colourless. In this colourless portion of the clot reticulated striæ and white spots are seen. On examining the clot microscopically, coagulation is found to be due to the formation of cylindrical fibrils and to granular laminæ anastomosing with one another and forming a network, in the meshes of which the red blood-corpuscles and the serum are entangled. The diminution of the size of the clot is owing to the retraction of the fibrinous reticulum, which, whilst keeping its hold on the red corpuscles, lets the fluid parts escape. It is difficult to distinguish the fibrinous reticulum in the midst of the red corpuscles. To examine it the clot must be hardened in alcohol and very fine sections cut, which after maceration in water should be cleaned with a brush. If a small fragment of a clot be acted on by water so as to dissolve out the red corpuscles without affecting the fibrin, the latter appears as irregularly anastomosing laminæ. In the colourless portions of clots formed slowly the fibrinous reticulum is more evident and more regular. The little whitish spots which are found in the colourless portion of the clot immediately above the layer composed of red corpuscles are caused by collections of white corpuscles entangled in a fibrinous reticulum.

Numeration of the blood-corpuscles.—Guided by the early researches of Vierordt, instruments have lately been designed by means of which numeration of the red and white corpuscles may be made fairly rapidly, and with tolerable precision.

The instrument for this purpose first invented by M. Malassez, and called by him The Capillary Corpuscle-counter (*Compte-Globules Capillaire*), consists of Potain's Mixer (fig. 28A) and a fine capillary tube. The mixer is a glass capillary tube, similar to that of a thermometer, and blown near one of its extremities into a small bulb, in which a glass bead is inserted. The long portion of the capillary tube is of such a length that its capacity is one hundredth that of the dilated portion. Two lines, drawn one below and one above the bulb, indicate the points which correspond exactly to these measurements. The long part of the tube ends in a point, the short part, the calibre of which is greater, fits into an india-rubber tube.

To obtain a solution of blood, the point of the tube is immersed in a drop of blood, and, by means of the india-rubber tube placed between the lips, the blood is sucked up the glass tube till it reaches the mark which separates the tubular from the dilated portion. Then, withdrawing the point and drying it, it is dipped into artificial serum,[1] which is drawn in till the bulb is filled as far as the mark indicating its upper limit. A solution is then obtained containing one part of blood in ninety-nine parts

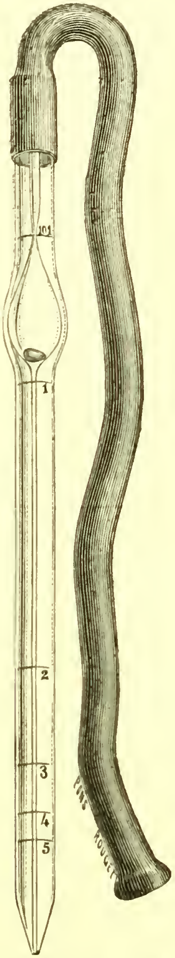

FIG. 28A.—POTAIN'S MIXER.

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[1] Artificial serum is composed of one part of a solution of gum arabic of a

of serum. The mixer shaken up and down, and the little bead thrown in every direction, aids in mixing the blood well with the serum. The solution is then introduced into the minute capillary tube. The calibre of the latter is written on the glass plate which supports it in figures which give the fraction of a cubic millimeter contained in a given length of the tube.

The microscope is graduated so that with a given lens and a given length of the tube of the microscope, the graduated micrometer in the eyepiece covers on a stage micrometer a number of thousandths of a millimeter, equal to one of the given lengths inscribed on the stage of the capillary instrument.

The fluid that is in the long portion of the mixer having been got rid of by gently blowing down the india-rubber tube, a drop of the solution is deposited on the plate of glass in front of the orifice of the capillary tube. The fluid penetrates by capillarity; if it does not, however, it may be gently aspirated by means of the india-rubber tube attached to the other end of the capillary tube. The fluid introduced and the microscope graduated as described above, the corpuscles found within the ruled space are counted. This number is multiplied by the figure written on the glass plate, which varies according to the length of tube selected. This figure expresses the fraction of a cubic millimeter given by the volume of the length of tube in which the corpuscles are counted. This latter figure must be multiplied by one hundred if the solution of blood and serum is at one per cent., and the number of corpuscles contained in a cubic millimeter of the blood examined is then obtained.

It is evident that this process does not give absolutely correct results, for an error made in the first numeration will be multiplied 15,000 or 20,000 times, but the results are sufficiently accurate for clinical use, and in each case they are of course capable of comparison.

M. Hayem uses a method very similar to that of M. Malassez. The solution is made in a glass vessel, into which is placed a known volume of serum measured by means of a pipette, and a smaller volume of blood measured by a second and smaller pipette. The solution of blood and serum are mixed together in the open air by

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specific gravity of 1,020, and two parts of a solution of sulphate of soda and chloride of sodium in equal parts, each having a specific gravity of 1,020.

A simple 5 per cent. solution of sulphate of soda at a specific gravity of 1,020 is found to be an excellent preservative, and is what is most generally used in these operations.—Tr.

a little rod of glass. A small drop of this solution is then placed in a cell $\frac{1}{5}$ millimeter or 200 μ deep. The drop is covered by a perfectly level cover-glass, at the edges of which a little water or saliva is placed to prevent evaporation. The corpuscles contained in a certain given area are then counted. This area is obtained by means of an eyepiece micrometer, which at a given length of the tube of the microscope corresponds to an area known beforehand. If, for example, the length of the micrometer is 200 μ, its surface represents a space of 40,000 μ^2. If the height of the drop is exactly 200 μ, the volume in which the corpuscles are counted is 200 $\mu \times$ 400,000 μ, that is to say of 0 mm., 008 or 125th part of a cubic millimeter. Thus, to ascertain the number of corpuscles found in a cubic millimeter of blood, the number of corpuscles found must be multiplied by 125 and then by the strength of the solution. M. Hayem's process is less exact than that of M. Malassez; it has, however, the advantage of being simpler, and the instruments are easier to keep clean.

In both of these instruments there is the same source of error to be pointed out. To collect the blood a puncture is made in the finger of the subject; during the time that must elapse between the formation of the drop of blood and the moment it is sucked into the pipette, evaporation takes place according to the temperature of the hand of the subject, and the time lost. To obtain comparable results, the puncture should be so made that a drop of blood of the same size is always obtained, and it should be collected in an identical period of time. But even then the temperature of the hand varies. To these sources of error another is added in Hayem's process. If a filament of any kind, or an atom of dust, is interposed between the slide and the cover-glass, the capillary space between these two will be increased, and a larger number of corpuscles will be calculated as existing per cubic millimeter.

According to M. Malassez's numeration there are in man, in the normal state, from four to five millions of red corpuscles per cubic millimeter. But this figure varies under different physiological and pathological conditions from 6,000,000 to 800,000. The mean number of white corpuscles ascertained by the same method is 8,000 per cubic millimeter, but they vary according to the vessel from which the blood has been taken and according to various physiological and pathological conditions.[1]

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[1] TRANSLATOR'S NOTE.—No mention is here made of Gowers's Hæmacytometer or of Malassez's new Corpuscle-counter, instruments of much clinical value. It has, therefore, seemed to me desirable to supplement the text by an extract from

In this summary we have only brought forward the most essential points of normal histology, and we now proceed to the study of pathological histology.

a critical notice of these instruments written by myself, entitled 'The Micrometric Numeration of the Blood Corpuscles,' and published in the *Quarterly Journal of Microscopical Science*, January 1881 :—

'In Gowers's Hæmacytometer,* which is a modification of Hayem's, a very decided improvement is made. In the depth of the cell and in the old-fashioned mode of mixing, it is identical with that of Hayem; the solution of blood used being, however, at 5 per 1000 instead of at 8 per 1000. The improvement consists in measuring the area and drawing the squares in which the corpuscles are to be counted upon the floor of the cell itself. Squares, with sides $\frac{1}{10}$ of a mm. long, are drawn on the floor of the cell. The area of each, therefore, is $\frac{1}{100}$ of a sq. mm. The cell having a depth of $\frac{1}{5}$ mm., and any 10 squares an area of $\frac{1}{10}$ of a sq. mm., the cubic contents of any ten squares taken within the cell will be—

$$\tfrac{1}{10} \times \tfrac{1}{5} = \tfrac{1}{50} \text{ mm.}^3$$

'The number of corpuscles observed in ten squares, therefore, multiplied by fifty will give the number in a cubic millimeter of the solution; and that multiplied by $\frac{1000}{5}$ will give the result for a cubic millimeter of blood.

'For example, if the number of red corpuscles counted on ten squares is 500, the calculation is simply

$$500 \times 50 \times \frac{1000}{5} = 500 \times 10{,}000 = 5{,}000{,}000 \text{ per mm.}^3$$

or, in other words, there is nothing to be done except to add 0000 to the number found by counting. No graduation of the microscope is required, so that the instrument can be used anywhere and with any lens. This renders it more convenient as a clinical instrument, and it is therefore that which is in general use in the English hospitals. It gives approximately accurate clinical results. I must, however, point out that it is liable to four serious sources of error, which destroy the value of observations made with it from an absolute and scientific point of view. These sources of error are—the uncertain depth of the cell; the inequality of the surface of the cover-glass; the method of placing the cover-glass on the drop; and the means used to make the mixture and to place the drop in the cell. Since a paper by two American physicians was published,† showing how careful observations may be vitiated by the variation in the depth of the cell, in different instruments, the error in the depth has been written on the slide. In the Hæmacytometer which I habitually use the cell has a depth of 190 μ, instead of 200 μ. This error necessitates a troublesome correction in each calculation. The correction is made by multiplying the number of corpuscles obtained by 20 and dividing by 19; for let a equal the number of corpuscles in a mm.^2 multiplied by the actual depth of the cell,

$$190\,\mu : a :: 200\,\mu : x.$$

This method of correction which is that recommended is, however, irksome when a great number of observations have to be made. I wish now to suggest that it may be altogether avoided by directing the instrument maker to graduate the pipette or mixer, whichever may be used, not, as at present, on the assumption that the depth of the cell accurately measures 200 μ, and therefore that a solution of 5 per 1000 should be used to insure correct results, but so to graduate it as to make a solution of such a strength that, having previously ascertained the actual depth of the cell, an area of $\frac{1}{10}$ mm.^{2} multiplied by this depth shall give $\frac{1}{50}$ mm.^{3} In this way the necessity for arithmetical correction of each observation is avoided, the special adjustment of the pipette affording a correction which applies to all observations made with the instrument. Thus, taking my own Hæmacytometer as an example, if, instead of using a 5 per 1000 solution, a 5 per 950 solution were used, *i.e.* 5 parts of blood to 945 of the diluting fluid, the result would be absolutely the same as if the depth of the cell were correct, or as if the error were corrected by calculation. Thus, supposing 500 corpuscles to be contained in ten of the squares,

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* 'On the Numeration of the Blood-corpuscles.' By Dr. Gowers. *Lancet*, Dec. 1877.

† 'Blood-cell Counting: a Series of Observations with the Hématimètre of MM. Hayem and Nachet, and the Hæmacytometer of Dr. Gowers.' By Drs. Henry and Naucrede. *Boston Med. and Surg. Journ.* April 1879.

$$500 \times 10 \times \frac{1000}{190} \times \frac{950}{5} = 5{,}000{,}000.$$

'This device will work equally well whatever the error in the cell may be, if the following rule be adhered to: Multiply the actual number of μ in the depth of the cell by 5 and take the product as the number of parts of the solution of blood and diluting fluid to be used, the number of the parts of blood remaining constant at five—

$$190\,\mu \times 5 = 950$$

or, still more generally, the number of parts of blood being fixed, and the actual depth of the cell in μ being known, the product of these two numbers, minus the number of the parts of blood, will give the necessary number of parts of diluting fluid required. With the pipette or mixer graduated according to these rules, it will only be necessary to add 0000 to the number of corpuscles counted in ten squares. I commend this suggestion to the notice of all who are using Gowers' instrument, as its adoption will greatly facilitate the attainment of correct results. Secondly, as to the error caused by the inequality of the surface of the cover-glass. Any ordinary cover-glass is used to flatten the drop to an uniform height. Now, as every histologist knows, cover-glasses are rarely of an uniform flatness; they are generally either slightly convex or concave, hence the layer of fluid is likely to be thicker in some places than in others, and consequently a count made in one part of the cell may give very different results from one made in another. To remedy this defect in my instrument, I have had ground a perfectly flat cover-glass. Thirdly, the mode of placing the cover-glass on the cell is faulty; whether it is dropped on horizontally or laid on gently at an inclined plane, the uniform diffusion of the corpuscles through the fluid is disturbed. Fourthly, in the method of mixing and placing the drop on the cell, errors are caused by the white corpuscles adhering to the sides of the vessels used for mixing, and by evaporation from the little open cup in which the solution is kept. Further, in placing the drop on the slide, unless the manœuvre is very quickly executed, the red corpuscles gravitate to the bottom of the drop, and are thus deposited and form a thicker collection in the centre of the drop than at the periphery. The white corpuscles also, by adhering to the glass rod, introduce a source of error in estimating the right proportion between white and red corpuscles. It is, I think, to be regretted that, in introducing this really useful clinical instrument, Dr. Gowers should have adopted the old, clumsy, and discarded method of making the solution, instead of using Potain's Mixer, the use and value of which were already known. By this mixer a solution of blood at 100, 200, 300, 400, or 500, as desired, is made in a *closed* vessel, evaporation thus being prevented; the drop is deposited on the slide whilst the corpuscles are in rapid motion and before they have had time to gravitate to the bottom of the drop. For the last eighteen months I have, when using Gowers's Hæmacytometer, substituted Potain's Mixer in the place of the apparatus provided, and with the result of obtaining much more uniform counts in different parts of the cell, whereas previously the want of uniformity was often very marked. By the means I have indicated, namely, by correcting the error in the depth of the cell, by substituting a perfectly flat cover-glass for one that may or may not be flat, and by using Potain's Mixer for making the solution, a useful and nearly accurate clinical instrument can be made of Gowers's Hæmacytometer. As it is at present arranged, the results obtained by it are often misleading, unless the mean of a great number of counts be taken. Single observations are likely to lead to the most fallacious conclusions, and are not at all trustworthy, whether for scientific or clinical data.

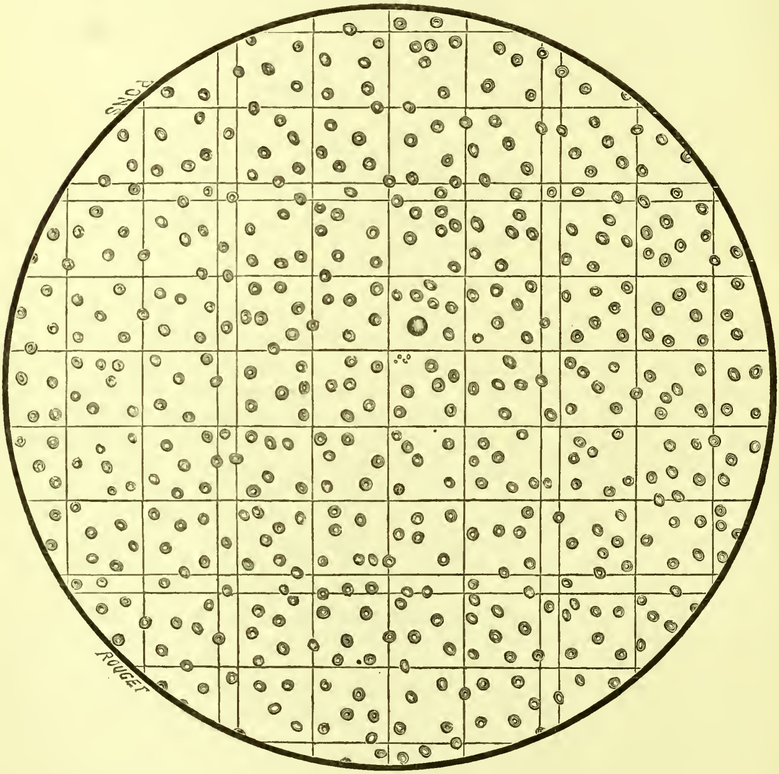

Fig. 1.—Appearance of the Corpuscles in the Ruled Space of Malassez's New Corpuscle-counter.

'In Malassez's new *Compte-Globules* he has adopted the great improvement introduced by Gowers, of drawing the squares on the surface of the slide. He has moreover succeeded, by many ingenious contrivances, in carefully avoiding all the sources of error in Hayem's and Gowers's instruments above enumerated, to several of which I had occasion to call his attention. This new micrometric graduated corpuscle-counter with wet chamber (*Compte-Globules à chambre humide graduée* *micrometrique**) consists of a thick nickel slide, in the centre of which is a circular groove enclosing a glass cylinder about a centimeter in diameter. Outside this groove are three pointed metal screws, equidistant from each other. The elevation of these points above the surface of the metal slide is exactly $\frac{1}{5}$ mm. In the centre of the glass surface, limited by the groove, are drawn the squares, in which the corpuscles are counted. These have a side of $\frac{1}{20}$ mm., and they are arranged in groups of 20, each group having a length of $\frac{5}{20}=\frac{1}{4}$ mm., and a width of $\frac{4}{20}=\frac{1}{5}$ mm., and an area, therefore, of $\frac{1}{5}\times\frac{1}{4}=\frac{1}{20}$ square mm. Each group of 20 squares is separated from adjoining groups by a double line (fig. 1). The peripheral parts of the ruled space are simply divided into rectangles, $\frac{1}{4}$ mm. long and $\frac{1}{5}$ mm. wide. The cover-glass, which is ground accurately flat, is attached, by moistening the edges slightly with saliva, to a frame fixed to the sides of the slide. By an ingenious and delicate rack movement of this frame the cover-glass is lowered without delay, and *in a horizontal position* down upon the drop. The slide carrying the frame is represented in fig. 2.

'To make a numeration, the solution is made in Potain's Mixer at the strength of 1 per 100, 200, 300, 400, or 500, as desired; and, whilst being rapidly agitated, a drop is placed in the centre of the ruled space, and the cover-glass, having been previously attached to the frame, is lowered and clipped, so as to rest firmly on the points of the screws. To prevent evaporation, if desired to keep the preparation any length of time, a drop of water should be placed at the edge of the cover-glass, and allowed to run under and fill the vacant space between its edge and the groove. The *red* corpuscles that are lying within a group of 20 squares are then counted. These 20 squares, it will be remembered, have an area of $\frac{1}{20}$ mm.^{2}, and, the depth of the fluid being $\frac{1}{5}$ mm., the quantity of the solution under review will be $\frac{1}{20}\times\frac{1}{5}=\frac{1}{100}$ of a mm.^{3} The number of corpuscles seen, therefore, has to be multiplied by 100, and then again by the number representing the strength of the solution, and the product will be as before, the number of corpuscles in a cubic millimeter of blood.

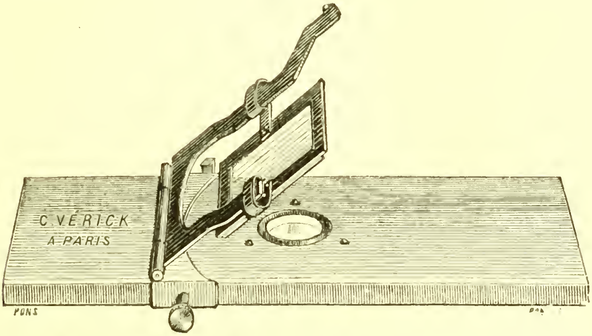

FIG. 2.—MALASSEZ'S MICROMETRIC GRADUATED CORPUSCLE-COUNTER.

'Thus, for example, let the solution be 1 per 200, and let 250 corpuscles be found on an area of $\frac{1}{20}$ mm.^{2}; then—

$$250\times 100\times 200=5{,}000{,}000.$$

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* 'Sur les Perfectionnements les plus récents apportés aux Méthodes et aux Appareils de Numération des Globules Sanguins, et sur un nouveau Compte-Globules.' Par L. Malassez. *Arch. de Phy.*

'Thus, to the number of corpuscles counted, if the solution be 1 per cent., it is only necessary to add 0000, but if the strength of the solution be less it is necessary to multiply the number of corpuscles by the figure representing the dilution before adding 0000. To correctly estimate the number of *white* corpuscles per cubic millimeter a much larger area must be taken, and for this purpose the rectangles of $\frac{1}{20}$ square mm. have been drawn on the slide. The number of white corpuscles found in ten of these large rectangles must be counted. If in a 1 per cent. solution the number of white corpuscles in ten of these large rectangles is found to be thirty, then we know, as above shown, that the volume of the solution counted is—

$$10 \times \tfrac{1}{20} \times \tfrac{1}{5} \text{ or } 10 \times \tfrac{1}{100} = \tfrac{1}{10} \text{mm.}^3$$

'The number counted, therefore, multiplied by 10 and then by 100, will give at once the number of white corpuscles in a cubic mm. of blood; or, in other words, it is only necessary, for a one per cent. solution, to count and add 000. For example:

$$30 \times 10 \times 100 = 30{,}000.$$

'This method of estimating the number of white corpuscles will be felt by every worker at this subject to be a great gain, for on this point none of the previous instruments gave any but the roughest approximate results, likely to give rise to the most delusive conclusions. To sum up, the advantages of this new *Compte-Globules* over that first introduced by M. Malassez are that it can be used clinically with any microscope, that no particular skill is required to use it, and only ordinary care to keep it clean and in order. Over other clinical Corpuscle-counters it possesses the merits—of making the layer of fluid accurately $\frac{1}{5}$ mm. in depth, so that there are no corrections to make; of having the squares ruled to the smallest size yet found possible, so that the numeration is exceedingly easy and not fatiguing to the eyesight; of making an exact computation of the number of white corpuscles per cubic mm.; and, lastly, by means of the rack movement of the carrier of the cover-glass, and by use of the Melangeur Potain, of preserving the homogeneity of the drop when placed on the slide and flattened to the depth of $\frac{1}{5}$ mm.'

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CHAPTER II.

GENERAL CONSIDERATIONS ON PATHOLOGICAL HISTOLOGY—MORBID CHANGES IN THE CELLS AND TISSUES.

Morbid Changes in the Cells and Tissues may be divided into two Groups: 1, Nutritive Changes simply; 2, Formative Changes consisting in the Formation of New Cells.

I.—Lesions of Nutrition of Elements and Tissues.

They may be divided in the following manner:—

A. Lesions caused by death of elements and tissues (necrosis).
B. Lesions caused by insufficient nutrition of elements (atrophy).
C. Serous and albuminous infiltration.
D. Mucoid and colloid infiltration.
E. Amyloid infiltration.
F. Accumulation of fat (adiposity) and fatty degeneration.
G. Pigmentation.
H. Calcareous infiltration.
I. Infiltration of urates.
J. Lesions caused by excess of nutrition.

A. **Lesions caused by the death of elements and tissues (necrosis).**—The death of certain elements is a physiological fact and sometimes even necessary to the performance of their function; for example, almost all epithelial cells are subject to incessant desquamation. It is probable that certain elements apparently permanent are destroyed at long intervals of time to be replaced by younger elements. This is what is observed in the muscular fibres of the frog, of which a certain number of primitive bundles are destroyed every winter (Wittlick) to be reproduced in the spring, according to the type of embryonic development. It is permissible to believe that analogous phenomena take place in the human body although here the destruction of muscular tissue has only been observed in serious disease, followed during convalescence by new tissue formation. When cells are formed in great numbers in consequence of irritation a certain number of them are destroyed because of deficient nutrition. This occurs whenever the supply of nutritive fluid is insufficient for the number of new elements. Of all the elements of the human body nerve cells and fibres have the longest term of existence; they energetically resist most of the pathological processes, and hitherto we are not aware of their physiological destruction. The death of histological elements occurs under two conditions: 1, in consequence of an arrest of circulation; 2, consecutive to an initial lesion of the cells.

1. *Death of the cells and tissues in consequence of an arrest of circulation.*—Whenever there is arrest of circulation in any part of the organism that part dies. Either suppurative inflammation takes place around it, or a kind of tolerance is established. The necrosed[1] part is decomposed, and slowly melts away into soluble particles which little by little are taken up by the circulation. In the latter case *infarct* and *necrobiosis* are said to occur, whilst in the first there is *eschar* and *gangrene.*

The phenomena which immediately follow **necrobiosis** are observed in the most delicate structures. The red blood-corpuscles lose their colouring matter, let their fatty substance escape in the form of granules, and finally break down into a granular detritus. Granules of a yellow, brown, or more or less brilliant red colour, and even rhombohedric crystals of a beautiful orange-red (crystals of hæmatoidin) may, after the lapse of some time, be found in the necrosed parts. Whenever blood is effused into natural or artificial cavities it undergoes similar changes.

The white corpuscles show a much greater resistance; they become dried up, granular, irregular, and angular fat granules and even sometimes pigment granules appear, and their nuclei and protoplasm melt into a common mass. This is what is called caseous change (desiccation and granular metamorphosis). Elements which have undergone this caseous change persist sometimes, under certain conditions presently to be described, for an extremely long period of time.

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[1] Contrary to general usage we make use here of the word necrosis in its general sense, which is that of death (*νέκρωσις* or *νεκρὸς*, death). The word necrosis thus understood is more general in its meaning than the word gangrene. The latter, in fact, expresses the idea of death, followed by decomposition, and elimination by suppurative inflammation.

Connective tissue, bone, cartilage, ligaments, &c., persist almost indefinitely in parts deprived of blood if the *gangrene is dry.* In this case the preservation of tissues, even those which easily undergo morbid changes, is owing to the fact that their constituent water evaporates and is replaced by fat escaped from fat cells. The fat impregnates the tissues as they become desiccated, and preserves them by preventing the approach of oxygen and water, which are necessary to the process of putrefaction. It is the infiltrated fat which gives translucence to sections made of dried and gangrenous parts, whilst the brown discoloration is connected with the presence of coloured granules proceeding from the colouring matter of the blood.

Moist gangrene occurs when the plasma of the blood continues to come in contact with the mortified parts, as is observed in gangrene consequent on inflammation, or on venous obstruction. When the gangrenous parts are deeply situated and cannot become dry, the gangrene is perforce moist; the fat forms into granules, but it cannot infiltrate tissues from which the water has not yet disappeared. If oxygen cannot reach the parts, as in cerebral ramolissement and in splenic infarctus, no putrefaction is possible, whilst on the other hand it takes place very quickly on the surface of the body and in the lungs where the presence of air favours this form of gangrene. Thus two phases of gangrene may be distinguished; that of *mortification*, and that of *putrefaction.* Examples of **mortification without putrefaction** may be often observed in the case of dead embryos which have remained for a longer or shorter time in utero. Some of these are almost dry and resist putrefaction better than any other tissue when exposed to the air after their expulsion. The following are the changes which are found in the elements and tissues in these cases. The red corpuscles are generally destroyed, but within the blood-vessels are found white corpuscles that have undergone caseous degeneration, previously described, round or angular pigment granules (hæmatin), and fat granules. The brain and spinal cord are reduced to a pulpy mass in which are found granules of fatty matter, crystals of cholesterin, and nerve cells, the nuclei of which are no longer visible. The nerve fibres have completely disappeared. The peripheral nerves are well preserved, excepting that the myelin, scanty at this age, is collected in the form of fine fat granules. The muscular fasciculi of the trunks and limbs contain no fat granules, but only brown pigment granules, derived probably from the colouring matter of the muscles. The muscular tissue itself, splendidly striated, is decomposed into its sarcous elements [1] or into disks in which the longitudinal striation is still very distinctly perceived. All the muscle fibres of the heart show, on the contrary, a certain number of fat granules. This preservation of muscular tissue after necrosis is frequent, and we have seen in an adult an infarct of muscle in which the tissue was nearly white, structure and striation being, nevertheless, perfectly preserved. The liver cells of the macerated fœtus are destroyed and replaced by a mass of albuminoid and fatty granules, fat crystals and pigment granules. All the cartilage cells contain a few granules of fat. The cells contained in the osseous corpuscles can be distinctly coloured with carmine and are well preserved, as well as the nuclei of the connective-tissue cells.

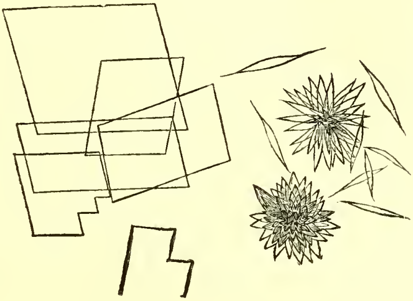

FIG. 29.—CRYSTALS OF CHOLESTERIN AND STEARIC ACID.
The crystals on the left are cholesterin plates.

In dry gangrene, as may be concluded from what has been said above, the tissues show analogous changes to those we have just been studying in the macerated fœtus; but in moist gangrene the ulterior changes occur rapidly, bringing about decomposition of the tissues, which are infiltrated with serum, or with pus from the neighbouring parts. Fibrous tissue, even the toughest, as that of tendons, ends by becoming dissociated into filaments.

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[1] This maceration is the only means known to us of obtaining at the same time dissociation of the muscular fibres in their longitudinal and transverse striæ. Chromic acid, alcohol, corrosive sublimate decompose the muscular fasciculus into longitudinal fibrillæ; acetic and weak hydrochloric acid decompose it into disks, but we do not know of any chemical substance combining these two properties at the same time.

Osseous tissue alone, at least the frame-work, persists for years without change. We have seen an example of necrosis of the humerus dating back authentically for thirty years, in which the osseous structure was preserved as in macerated bone, that is to say, the living cells had disappeared from the osseous corpuscles, but the laminæ and the stellate bodies were perfectly preserved. In these cases, however, the surface of the bone is blackened, this is due to the presence of sulphate of iron, the iron proceeding from the blood, the sulphur from decomposed albuminoid material.

In moist gangrene the ulterior metamorphoses of fat give rise to crystals of margarin, stearic acid, and cholesterin. Crystals of leucin and tyrosin, which are almost constantly present, are probably derived from albuminoid substances. Finally, angular granules, together with brown or black crystals derived from red blood-corpuscles, are met with, these are produced from hæmatin or analogous colouring matter.

2. *Mortification of the tissues by initial change in the cells.*—Death of the tissues may be due to an initial change in the cells. This is what occurs in primary fatty degeneration of the cells such as is seen in atheroma of the arteries, caries, &c., and in degenerations consecutive to inflammation. A great number of cells dying, the tissue, which is made up of them, dies also. Various phenomena succeed; an actual elimination of the mortified parts by inflammation of the peripheral tissues may occur as in caries. Sometimes the mortified part remains in its normal position and becomes infiltrated with calcareous salts, as is observed in atheromatous plaques of the aorta; or at last the mortified part may soften, break down, and be taken up by the circulation.

B. Lesions caused by an insufficient nutrition of the elements (atrophy).—Atrophy from insufficient nutrition has been studied much more in relation to the organs than with regard to the elements and tissues. Very few examples are known of atrophy of the elements not related to some one of the processes of degeneration to be studied further on.

Atrophy is physiological under the following circumstances: in embryonic development a certain number of vessels, the umbilical artery and vein, the ductus arteriosus, &c., become atrophied. The thymus undergoes similar changes during the first years of life, but here fatty, colloid, or calcareous degeneration is most often observed. The genital organs atrophy in old age. In man the genital function is continuous, whilst in certain animals in which it is intermittent, the genital glands are seen to undergo considerable atrophy after the period of rut. The uterus, which during gestation is provided with muscular elements of great size, undergoes involution after parturition. The muscular elements diminish in size, whilst they undergo at the same time destructive fatty degeneration. There is here, therefore, a combination of simple atrophy and of atrophy with degeneration. The ovaries, after the menopause, atrophy throughout their entire mass, and the fibrous tissue of the organ becomes condensed. The testicles in old age atrophy by the epithelial elements undergoing fatty degeneration.

It is seen from these examples what intimate bonds unite atrophy of the organs with various kinds of degeneration of their elements. Atrophy of the mammæ is an exception to this rule. Here, in fact, after the cessation of lactation shrinking of the acini is accompanied by simple atrophy of the pavement cells which line them. In old age a certain number of glands atrophy, whilst others, as the kidney, become condensed. The uriniferous tubuli are smaller than in the normal state. Some of them are obliterated by colloid masses, thus giving rise to small cysts, &c. The liver and spleen are also smaller, whilst their fibrous capsule is thickened. In old age the muscles constantly show a certain number of fasciculi atrophied and in a state of fatty degeneration.

Typical pathological atrophy of elements, without any particular degeneration, is met with chiefly in emaciation consequent on inanition and acute or chronic disease. The muscular fasciculi then diminish in thickness whilst their structure is preserved. The adipose cells lose a part of their fat and retract, the drop of fat which occupied the centre of the cell diminishes in size, it may even entirely disappear, the size of the cell being still preserved by its being filled with serous fluid. This is observed in œdema of subcutaneous cellulo-adipose tissue coexistent with emaciation. In this case the cellulo-adipose tissue is gelatiniform and transparent. Irritation of the cellulo-adipose tissue ends also in the absorption of the fat, when the protoplasm and nuclei of the cells become more swollen and apparent than in the normal state.

Atrophy may be accidentally the consequence of the compression which different organs and tissues exercise on each other. Thus, in the kidney, when the pelvis is distended into a single cyst, by pyelitis, hydronephrosis, or a tumour, and the renal tissue is flattened so as to form the wall of the cyst, the uriniferous tubuli are found extremely narrow, their epithelial cells atrophied and generally in a state of fatty degeneration. A similar atrophy takes place in the cells of the liver when compressed by new tissue in interstitial hepatitis or tumours of this organ. Hypertrophy of the interstitial tissue of organs generally leads to atrophy of their parenchymatous elements. This occurs in the muscles, heart, testicles, kidney, &c.

The possibility of primary atrophy of the parenchymatous elements, as occurs in certain forms of muscular atrophy, must also be taken into consideration. In such cases interstitial connective tissue and cellulo-adipose tissue take the place of the atrophied parts, filling up the spaces atrophy has caused, so that even an apparent hypertrophy of the organs may result from increased deposit of fat. This may be observed in certain muscular paralyses.

We have given this sketch of widely differing forms of atrophy in order to bring out clearly the relations between atrophy of organs and that of their elements, and to show that atrophy of the latter is rarely simple but is almost always connected with consecutive degeneration.

C. **Serous and albuminous infiltration.**—We have just seen how that in the atrophy of fat cells they may undergo serous infiltration, and we have noticed that this lesion is met with in cases of emaciation and of irritation of the elements. It is probable that the composition of the infiltrate is not the same in the two processes, but we can only distinguish one from the other by the fact that the nucleus and protoplasm swell in inflammation.

Whenever a slight irritation exists or there is an increased influx of nutritive fluid into the epithelial tissues, the epithelial cells swell and are filled by an albuminous fluid containing fine granules soluble in acetic acid. This is what is called cloudy tumefaction of the cells. The nuclei and nucleoli may also present similar changes. Thus the nuclei of the cells of the Malpighian layer may be filled with fluid and become of a decidedly vesicular form.

The muscular fasciculi undergo a similar change; they become tumefied, infiltrated with a granular albuminous substance; between this state and that described by Zenker under the name of *waxy degeneration* every intermediate condition may be observed. The waxy degeneration of Zenker, perfectly well known from its physical characters, is not sufficiently known from the chemical point of view. It is not known if it is simply a serous or albuminous infiltration, or a colloid transformation with which, as we shall presently see, it presents certain points in common. We may say as much of an alteration of the epithelial cells of the mouth, pharynx, larynx, and trachea, described by E. Wagner, and which constitutes an important lesion in diphtheria (*vide* p. 104).

In œdema, whatever may be its cause, there is serous or albuminous infiltration of the areolar connective tissue, the exuded fluid filling the spaces between the fasciculi. On puncturing this tissue fluid flows freely, for, the inter-fascicular spaces being artificially distended, they necessarily communicate with one another. In this state preparations of connective tissue are easily made, it being sufficient to remove a portion with scissors, place it on a slide, and cover with a cover-glass. The fibres are then seen to present no morbid change. It is not the same, however, with the connective-tissue cells. These cells, which in their normal state are flattened and show more or less elongated processes, are now tumefied and nearly globular in shape and in their substance there are albumino-fatty granules. Similar granules are developed in the marginal protoplasm of the fat cells. The lymph cells, which, as is well known, travel in the normal state between the connective-tissue fibres, are here found in much larger numbers. In œdema of the lung, serum is effused into the alveoli, which, from the morphological point of view, are the analogues of the lacunar cavities of connective tissue.

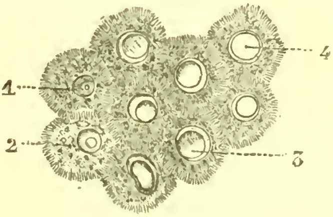

FIG. 30.—EPITHELIAL CELLS OF THE MALPIGHIAN LAYER IN A CASE OF SLIGHT IRRITATION.

The nuclei have become vesicular by dilatation of their nucleoli. 1. Nucleus and nucleolus in a normal state. 2. Nucleolus dilated. 3 and 4. The same change a degree more advanced.

D. Mucoid and colloid infiltration.—If mucus or synovial fluid be treated by acetic acid, a white stringy precipitate is thrown down which is not redissolved in an excess of the same acid. Virchow has given the name of *mucin* to the substance thus precipitated. Alcohol precipitates mucin as well as albumen, but the precipitate of mucin swells in water. Mucin is elaborated by certain epithelial cells of the mucous membranes and by the cells lining synovial membranes. In fact a fluid possessing the same characters as this substance may be found in the interior of these cells.

A gelatinous *colloid* substance is further recognised in the organism. It is of greater consistence than mucin, and also results from a physiological elaboration within cells. It is chiefly to be found in the thyroid body. In the follicular cavities of that organ are seen refractile masses, the product of the cells which line the follicles. These cells appear to elaborate this colloid substance by a physiological process of degeneration, ending in their own destruction. Colloid substance is easily stained red with carmine; the staining is permanent, and is more intense than that of the cells and intercellular substance, though less strong in colour than that of the nuclei. Acted upon by acetic acid it does not swell, or only slightly, and has not a granular appearance. Colloid substance also differs from mucin in that it is not precipitated by acetic acid. Colloid is so nearly related to albuminoid substance, that Virchow has succeeded in producing it artificially, by treating serum of blood with calcined common salt. Between mucoid and colloid substances there are many intermediate forms, thus rendering it difficult in every case to distinguish one from the other, which fact justifies our description of them in the same chapter.

To mucoid degeneration is referred the softening and destruction of the matrix of the costal cartilages in old age. Starting from this solitary fact, some observers, Rindfleisch among others, have supposed that when the matrix is destroyed so that the cells are set free, mucoid degeneration is always the cause. But this supposition is not supported by adequate observation. There is no example of pathological mucoid or colloid degeneration which does not find its analogue in types of physiological evolution of mucin and colloid substance, such as we have just described.

Mucus or colloid substance is elaborated within the cells. It is observed in the epithelial cells of mucous membranes affected with catarrh. It appears in the form of globular masses round the nucleus, or beside it in the protoplasm. When this substance accumulates in the cell, the nucleus is pushed to the periphery, as is seen physiologically in *chalice* cells. According to Förster—and we are of his opinion—a part of the bodies called *physalides* by Virchow result from colloid transformation of cells. Colloid globules formed in the midst of cells may show concentric layers. They are easily stained with carmine, and sometimes retract when acted upon by acetic acid. We shall see later how they may be distinguished from calcareous, amyloid, and fat globules. The secretion of mucin is increased in catarrhal or superficial inflammation of mucous membranes, particularly in acute rheumatism. This is in relation with a greater activity of the cells.

The exaggerated formation of colloid substance acquires its maximum intensity in certain tumours of the thyroid body, called *goitres*. In fact, in certain kinds of goitre there is nothing more than an excessive formation of colloid substance, terminating in the production of more or less voluminous cysts, possibly communicating with each other. Colloid transformation of cells is sometimes observed in the lymphatic glands of old persons. In such cases all the lymph corpuscles of a follicle become colloid, and numerous cysts are produced, comparable to the follicles of the thyroid gland of the adult. In the kidney, particularly in old age, certain cysts are filled with a colloid substance apparently secreted

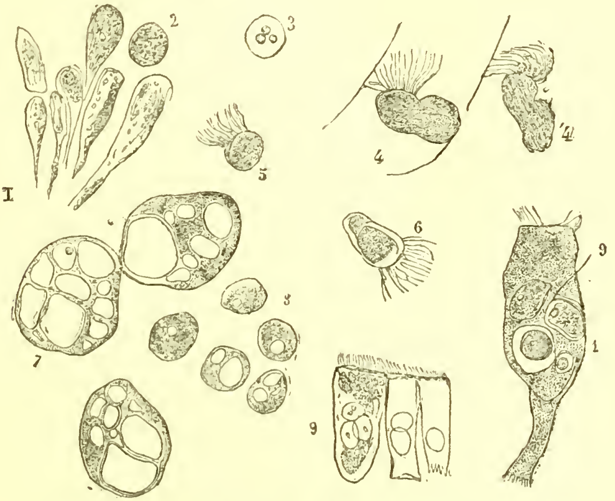

FIG. 31.—CELLS UNDERGOING MUCOID DEGENERATION.

Taken from the mucous membrane of air passages affected with catarrhal inflammation. 1. Mucoid degeneration in cylindrical cells. 2. Pus-cell. 3. The same treated by acetic acid. 4. Cylindrical cell, the cilia of which are vibrating. 5, 6. Small round ciliated cells, the body of which resemble pus-cells. 7, 8, 9. Cells undergoing the mucoid degeneration of coryza, from the nasal passages. Magnified 450 diameters.

by the epithelium of the tubuli. The latter dilate and are transformed into cysts, the centre of which is occupied by a colloid mass, festooned at its borders, and showing cells undergoing a process of degeneration similar to that in the thyroid. The so-called fibrinous casts of Bright's disease seem to be formed of a substance analogous to that of these cysts, having the same refractive index, the same readiness to stain with carmine, and similar resistance to the action of acetic acid.

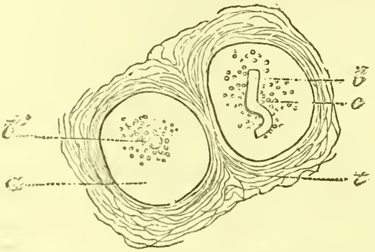

FIG. 32.—SECTION OF TWO CYSTIC URINIFEROUS TUBES FILLED BY COLLOID SUBSTANCE, *a*, IN THE MIDST OF WHICH HYALINE CASTS OF THE SAME NATURE ARE SEEN, *b*, *b'*. MAGNIFIED 100 DIAMETERS.

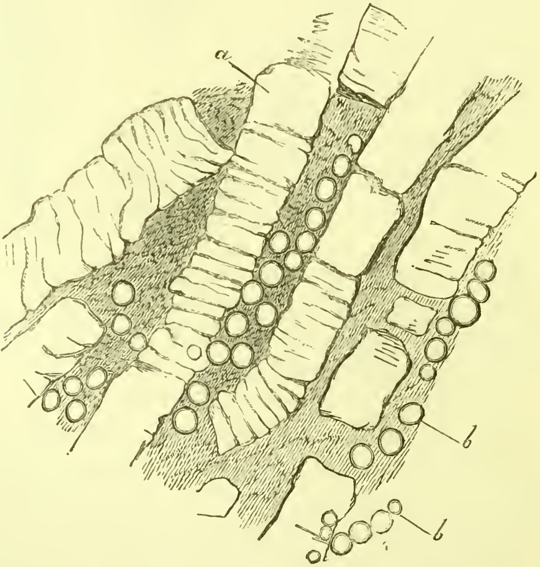

FIG. 33.—MUSCULAR FIBRES UNDERGOING VITREOUS DEGENERATION.

a, degenerated fasciculus; *b*, fat. Magnified 300 diameters.

We may connect with colloid substance the *vitreous degeneration* of muscles (waxy degeneration of Zenker). Here the muscular fibres swell and become transparent; they present transverse and longitudinal fissures; the new substance which brings these physical changes about is stained with carmine, and swells slightly by the action of acetic acid, which causes the fissures to disappear. This morbid change is observed in typhoid fever, and in many affections of the muscles from whatever cause (eruptive fevers, tumours, abscesses, &c.).

Similar changes are found in the epithelial cells which have undergone the so-called fibrinous degeneration of Wagner, an important lesion of mucous membranes attacked by diphtheria. The cells obtained by the dissociation of diphtheritic pseudo-membranes have a vitreous, transparent appearance, they show processes, and are easily stained with picro-carminate of ammonia, and are very slightly distended by the action of acetic acid.

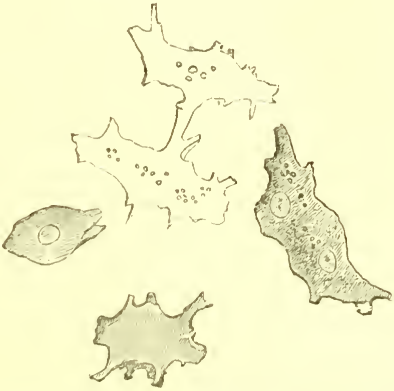

FIG. 34.—EPITHELIAL CELLS FROM DIPHTHERITIC FALSE MEMBRANE.

In tumours (epithelioma, sarcoma, carcinoma, &c.) mucoid and colloid degeneration of cells is very common. When present, the cellular elements and the tissue undergo destruction, causing the formation of irregularly shaped cavities full of mucus, which mucus may be extracted and tested by reagents. This lesion is very common in sarcoma, carcinoma, fibroma, myxoma, &c. In certain forms of epithelioma, and sometimes in cysts, the characters of colloid substance may be recognised. Mucoid and colloid degeneration may thus form a variety in each class of tumours.

E. Amyloid infiltration.—The name of amyloid substance is given to an albuminoid material which, sometimes deposited in the form of spheres with concentric layers, sometimes infiltrating cells and tissues, has the property of staining mahogany-red colour with iodine. However weak the solution may be that is employed, this substance is strongly coloured, whilst the surrounding tissues are hardly tinted yellow. Often after staining with iodine, a blue, green, or violet colour is obtained on adding sulphuric acid. With methylanilin violet or Paris violet (Lauth's violet), the parts attacked by amyloid degeneration may be as well defined as with iodine. Hoffmann's violet shows the same reaction. All that is required is to have a highly coloured solution of these reagents, and to stain a thin section of the specimen in the fresh state, or after hardening in Müller's fluid, picric acid and alcohol. On contact with the preparation the violet is split up into two colours, red-violet and blue-violet; all the amyloid parts are coloured red-violet, whilst the normal parts are coloured blue-violet. This splitting up is perfectly distinctly seen in the most delicate elemental parts, for instance in the fibrillæ and granules as well as in the cells. Thus the situation of the amyloid substance may be studied in every detail.

This substance exists physiologically in the prostate in masses showing concentric layers, and in granules of variable size. Also as little spherules in the central nervous system, principally at the periphery of the spinal cord and on the surface of the brain. Without employing iodine and sulphuric acid it is often impossible to say whether colloid or amyloid substances are under examination; they have, in fact, both the same index of refraction, and colloid spherules are also often arranged in concentric layers.

Pathologically, amyloid material infiltrates various elements. It is diffused through cells, and finally destroys them. They lose their nuclei, and are transformed into amorphous blocks of variable size: such are often seen in the liver and spleen. But the tissue most subject to this kind of degeneration is the smooth muscular tissue of the small arteries and the walls of capillaries. When cells undergoing amyloid degeneration are arranged in such a way as to encircle a canal, for example round blood-vessels and uriniferous tubuli, they become fused, and melt into a common amorphous mass; the membrane of the canal is very much thickened, the cells become tumefied, and unite in such a way that the calibre of the blood-vessels and uriniferous tubes becomes in certain cases much narrowed. Amyloid corpuscles are always produced in the brain and spinal cord in chronic inflammation of these organs.

Amyloid substance is also met with in the form of diffuse infiltration, in the elements of the liver, spleen, kidney, lymphatic glands, vessels of the intestine and of the lung, and very frequently in chronic suppuration, particularly if the suppuration is related to scrofula, tuberculosis, or syphilis.

F. Adiposity or deposit of fat, and fatty degeneration.—Fatty substances are met with in the body in two states. They may be in intimate combination with other substances, separation not being possible except by chemical analysis, as in fat entering into the composition of the elements, or fat may exist, as seen under the microscope, in the form of granules or droplets.

The causes which induce constituent or latent fat to become apparent are not yet well known. It has, however, been ascertained that death of certain cells is sufficient to make fat apparent. On this subject we refer the reader to what we have said regarding the appearance of fat in the viscera of the macerated fœtus in utero (p. 61). Fat granules appear under the microscope as spherical bodies of variable size. They are highly refractive, transparent, colourless or slightly yellow, and, seen by transmitted light, bordered by a dark line. Fat is insoluble in acetic acid and in a 40 per cent. solution of potash, but it dissolves in an excess of ether and in sulphide of carbon. It is not stained with carmine, but is coloured brown with iodine and black with osmic acid. If fat remains long in the organism and is no longer subjected to nutritive changes, it breaks up into fatty acids and cholesterin. Stearic acid (fig. 29) crystallises into rhomboidal needles, isolated or radiating from a central point like the fruit of the Spanish chestnut. The more important crystals of cholesterin take the form of extremely delicate rhomboidal plates, of which one or more angles are often cut off by a notch whose borders are parallel to the corresponding borders of the crystal (fig. 29). They are coloured red with concentrated sulphuric acid, and blue if previously coloured brown with iodine and then treated by sulphuric acid.

Fat seems always to be deposited in the protoplasm of cells. In the muscular fasciculi the deposit commences round the nuclei, and is continued in the longitudinal grooves, which are also composed of cellular protoplasm. Whenever fat is found free in the tissues, it indicates that the cells have been destroyed. If, however, the examination is made in dessicated preparations, free fat is found in considerable quantities, without destruction of the cells. This is owing to the fact that fluid fat fills all the interspaces from which the water of composition has been driven by evaporation.

Physiologically and pathologically, fat may be seen under two conditions: either it fills the cells, these not having ceased to live —it is then adiposity or deposit of fat; or the cells invaded by fat are destroyed—this is fatty degeneration or necrobiosis. It is probable that at the same time the anatomical elements undergo other modifications of nutrition which render life impossible.

Adiposity or Deposit of Fat.—Adiposity is met with physiologically in the cells of the cellulo-adipose tissue; in proportion as the individual puts on fat, fresh connective-tissue cells become filled with fat. The cells of the liver and of the supra-renal capsules are also often physiologically the seat of fat granules or droplets. In the liver particularly they are met with in large quantities after a meal. In women who are suckling, as well as in all female animals during lactation, the hepatic cells are surcharged with fat, so that the liver seems to be the storehouse of the fat destined to the mammary gland for the purpose of milk secretion. The epithelial cells of the intestinal villi are also charged with extremely fine granules of fat during digestion. Permanent cartilage cells physiologically show more or less abundant accumulation of fat. The excessive production of fat in the liver, polysarchia, and the formation of adipose tissue between the muscular fasciculi in certain paralyses or in the place of an atrophied organ, are examples of deposit of fat. The fatty infiltration of the liver in phthisical patients seems to us to be

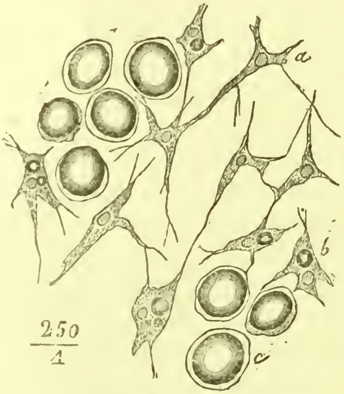

FIG. 35.—LIPOMATOUS MYXOMA.

The cells of the mucous tissue are filled with fat. *a*, normal cell; *b*, cell containing a droplet of fat; *c*, cell completely filled by a large drop of fat.

explained by hindrance to the pulmonary circulation and by the increase of respiratory combustion.

Fatty Degeneration.—Examples of physiological fatty degeneration are numerous; they are chiefly met with in the glands where fat is one of the products of secretion, for instance in the sebaceous, ceruminous, and mammary glands. In the sebaceous glands the fat, visible in the form of granules within the cells, is soon set at liberty by the destruction of the cells themselves. The fatty degeneration of the hypertrophied muscle cells of the uterus after parturition, and that of the cells of the Graafian follicle in the *corpus luteum*, are also physiological phenomena. In old age also numerous fatty changes are seen. Such is simple atheroma of the internal and middle coats of the arteries and the fatty degeneration of certain primitive fasciculi of the muscles of the limbs and heart; such, again, is the *arcus senilis* of the cornea.

Pathological fatty degeneration is constantly observed in poisoning from phosphorus, arsenious acid, antimonial and mercurial salts and mineral acids. When circulation is arrested in a limited part of an organ causing local death, such as generally occurs in infarcts and particularly in brain softening, the elements of the affected region undergo fatty degeneration. In the last stage of all neoplasms, inflammatory or otherwise, when the fluids brought by the circulation are insufficient for the nutrition of the cellular elements, newly formed in such abundance, a part or the whole of these cells undergo fatty degeneration. Primitive fatty destruction of unknown cause is seen in the bone corpuscles and in the cells of articular cartilage in caries of the bone and in white swelling of the knee.

If now we attempt to explain fatty degeneration of the elements in these different conditions, we find first that fatty change may be consecutive to death of the elements by arrest of the circulation; the constituent fat of the cells is then set free and becomes apparent. Starting from this fact, we can understand what occurs in elements which are no longer subject to nutritive changes, though they may be situated in the midst of living tissues, and enjoy all the normal conditions of moisture and temperature.

In all infectious diseases analogous lesions may be seen in the different viscera.

To demonstrate the pathogenesis of fatty degeneration we have had recourse to the following experiment, which we have repeated several times. A morsel of pith is placed in the cellular tissue or in the peritoneum of an animal; the foreign body sets up suppurative inflammation, and pus cells penetrate into the cells of the pith by traversing its porous canals. In the frog, at the end of a few days, pus cells are found in four or five layers of the pith cells. Some show amœboid movements, and have no fat granules inside them; others preserve their globular form, and show fat granules. Finally, alongside them quantities of fat granules are found immersed in an albuminoid mass. By this it is seen that pus cells removed from the conditions of normal nutrition very rapidly undergo fatty degeneration. An analogous process leads to the fatty degeneration of the products of inflammation and of pus, particularly when the cellular elements are numerous, crowded together, and insufficiently nourished.

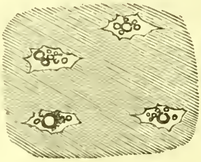

Fig. 36.—Osseous Corpuscles which have lost their Nuclei and contain Fat Granules.

From a case of caries.

Although in these cases it is certain that the fat proceeds from pre-existing cellular elements in which it was masked during their life, it is not the same in case of poisoning and infectious diseases. Here, in fact, the quantity of fat is often considerable, and it seems evident to us that there is a greater afflux of fat than in the normal condition, or a more active elaboration of fat by the elements themselves. Some histologists, Förster in particular, think that albuminoid substances may, within the

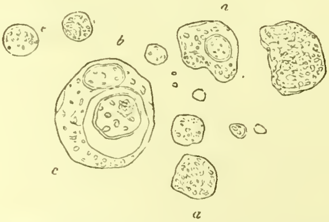

Fig. 37.—Elements infiltrated with Fat Granules.

From a case of tubercular pneumonia.

organism, give origin directly to fat, and even go so far as to say that an albuminoid granule may become a fat granule. We do not know of any microscopical observation justifying this view.

From the preceding it is apparent that the question of fatty changes is far from being definitely solved. In regard to each of the facts, hypotheses may be put forward, which, however, are not distinctive. They are as follows :—

1. Latent fat may become apparent in consequence of an impediment to or an arrest of nutrition.

2. Excess of fat may be supplied by the blood, in which it is always physiologically present.

3. A more active elaboration of fat by the cells may occur, a property which cartilage cells, removed from the circulation of the blood, may be shown to possess.

4. The fat in the cells may not be reabsorbed by the blood-vessels. In fact, when the circulation is stimulated, fat already present in cells disappears very readily, as may be seen in inflammation and in the emaciation of fever.

We shall return to the important phenomena of fatty degeneration and their physiological explanation when treating of each of these cases.

G. **Pigmentation of the elements and tissues.**—Under this title are included the extremely various changes which consist in the production of red, brown, yellow, and black granules in the cells and tissues. These coloured granules may be imported from without ready formed as occurs with vegetable carbon ; or they may be produced by a soluble colouring matter, such as is contained in the blood or bile, infiltrating a cell and forming a concretion there ; or coloured particles may be elaborated by the cell itself.

Penetration of particles of carbon is well established by the black pigmentation of sputa cells, when air charged with lamp-black has been breathed. Traube has seen particles of carbon showing the characteristic porous canals of vegetable cells in the interior of epithelial cells from the lung. In the conditions under which we live the cells and connective tissue of the lung of every adult contain more or less carbon. Formerly the presence of foreign substances in the interior of cells was explained by the supposition of the formation of a cell enveloping the primary coloured particles. It was thus that Kölliker explained the large cells in the spleen containing red blood-corpuscles. It is now known that cells simply formed of protoplasm and capable of amœboid movements may directly englobe granules and small fragments found in their neighbourhood.

Physiological pigmentation of cells by the colouring matter of the blood is observed in the spleen; normally also in the splenic tissue large cells are found containing red blood-corpuscles, and red, yellow, and black pigment. The colouring matter of the bile which is found physiologically, in small quantities, it is true, in the hepatic cells, is probably also the product of the red blood-corpuscles destroyed in the liver by the biliary acids. The facility with which the biliary acids destroy the red corpuscles is well known, and, moreover, amorphous granules and crytals of hæmatoidin from the blood are not distinguishable morphologically and chemically from granules and crystals of cholepyrrhin (Brücke and Zenker). The formation of the *corpus luteum* in the ovary, after the escape of the ovule and hæmorrhage into the Graafian follicle, is an example of the formation of red pigment, and later on of black pigment, when the *corpora lutea* appear as little slate-coloured cicatrices.

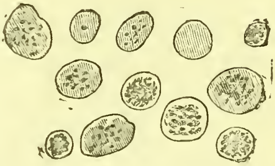

FIG. 38.—PIGMENTATION OF THE ELEMENTS OF SPUTA.

Whenever blood is effused, the connective-tissue cells and the endothelial cells of the serous membranes, and generally all the neighbouring cellular elements, are impregnated with a fluid containing hæmoglobin in solution, which, becoming decomposed and solid, forms granules of hæmatin and crystals of hæmatoidin. When muscular tissue dies its colouring matter solidifies in the manner we have already indicated.

Pathologically, these facts were first carefully studied by Virchow in connection with pulmonary hæmorrhage. He noticed that epithelial cells, after becoming spherical and impregnated with coloured fluid, soon showed among their contents yellow and red granules, which grew more and more deeply tinted, and also crystals of hæmatoidin. This observation led Virchow to the hypothesis that the colouring matter of the blood discharged from the red blood-corpuscles first infiltrates the cells as a coloured fluid; but that it may also form coloured granules outside the cells, which may subsequently penetrate their interior.

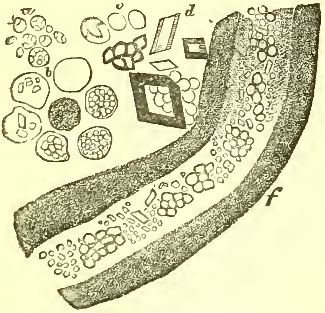

FIG. 39.—CRYSTALS OF HÆMATOIDIN.

a, red blood-corpuscles in a granular state and beginning to become decolorised; *b*, cells of the neuroglia, some of which have pigment granules and crystals in their interior; *d*, crystals of hæmatoidin; *f*, an obliterated vessel; its former channel is filled with red, granular and crystallised pigment. Magnified 300 diameters.

Yellow, red, and brown pigment granules are characterised particularly by their colour; sometimes they are so large that they may be almost perceived by the naked eye; in other cases they are so small that the highest powers must be used to recognise them.

Normally, the connective-tissue cells of the choroid, iris, and pia-mater, the epithelial cells of the retina and of the *rete mucosum* of the coloured races, the muscle fibres of the heart and the nerve cells contain pigment granules, which are brown originally and distinguishable by that very fact from the granules derived directly from the colouring matter of the blood. These granules are small and generally round; they are almost always distributed evenly round the nucleus in the protoplasm of the cells, but they may be also present in the nucleus itself, as may be seen in the *rete*

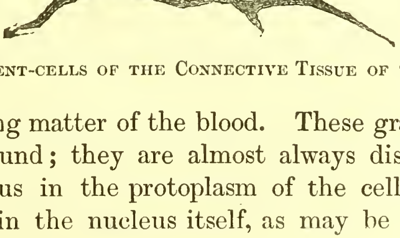

FIG. 40.—PIGMENT-CELLS OF THE CONNECTIVE TISSUE OF THE CHOROID.

mucosum of the skin of negroes. Pigmentation of the coloured races is in relation with a certain activity of the skin excited by the solar rays.

Pathologically, black pigment seems to be the result of a special cell elaboration; in fact, this pigment may be produced far from the vascular system, and the granules appear black from the first without passing through the intermediate hues of yellow and red. Pathological formation of black pigment may take place in the existing cells of tissues, producing simple melanosis, or in cells of new formation, as may be observed in melanotic, sarcomatous, or carcinomatous tumours.

H. **Calcareous infiltration.**—Calcareous deposits are composed of carbonate of calcium and tribasic phosphate, with three equivalents of lime ($PhO^5 3CaO$). These two salts are combined in calcareous deposits, with the exception of otolithes, which are solely composed of carbonate of lime. Osseous tissue, properly so called, must not be confounded with tissues infiltrated with calcareous salts. In bones, collagenous substance and calcareous salts seem to be combined in certain proportions to form the lamellæ, which have a definite structure. Calcareous concretions, on the other hand, consist in the infiltration of some albuminoid substance with lime salts. When these salts have been removed by hydrochloric acid, the infiltrated substance shows no relation to the structure of true osseous tissue. When calcareous salts are deposited in the tissues, they appear as isolated granules, or as spherical bodies with concentric layers, or they may give the appearance of true petrifaction. The granules are round or angular, and highly refractive; when small and massed together, they cause considerable opacity of the tissue; if, on the contrary, complete petrifaction exists, the tissue is as transparent as arragonite. If a thin layer of petrified tissue be ground down, yellowish transparent preparations are obtained, in which, on microscopic examination, lacunæ, fissures, and granules are recognised. The lacunæ and fissures are in relation with the structure of the primitive tissue. They appear opaque, as they contain the *débris* or altered elements of this tissue, and often isolated calcareous granules.

All acids dissolve calcareous salts by liberating carbonic acid gas. The acids generally used are hydrochloric and sulphuric acid. Hydrochloric acid causes the disappearance of calcareous salts without leaving any traces; sulphuric acid, whilst dissolving them, determines the formation of acicular crystals of sulphate of lime. By the action of these acids the tribasic phosphate of lime is changed into soluble acid phosphate of lime. Each calcareous granule, after the lime salts have been dissolved out, leaves an albuminoid framework behind, in which it is possible to recognise concentric layers if such was the arrangement of the concretion.

Physiologically, isolated calcareous granules are observed in the matrix of cartilage during the first phase of ossification. Globular calcareous concretions with concentric layers are met with in the choroid plexus of the adult, often also in the thymus gland during its retrogressive period, and in the meninges of the brain and spinal cord in old age. Petrifactions are also found in the adult in the deep layers of cartilage situated near osseous tissue, and in the costal and laryngeal cartilages of old persons. Calcareous infiltration never commences in the interior of cells, but always in the ground substance surrounding them. Subsequently the cells may be invaded, but they resist for a long time.

Pathologically, calcareous granules are met with in cases where a part remains long in the midst of living tissues, being itself no longer alive.

Examples of this have been observed in the case of extra-uterine gestation of twenty years' duration, in old long-standing infarcts, and in caseous masses, particularly when in the lymphatic glands. These belong to one category of facts. Calcareous concretions are met with in retained secretions of the salivary glands, the acinous glands of the pharynx, the pancreas, the lymph follicles of the tonsils, in the articulations and synovial sheaths, and in the interior of all cysts, particularly colloid cysts, of the thyroid and kidneys. They are the result of the infiltration of the products of an abnormal or vitiated secretion of these organs, and are of irregular shape, or arranged in concentric layers. In old centres of chronic inflammation, particularly in endo-arteritis, calcareous granules or petrified plaques are found. These changes only take place when the inflamed tissues have lost vitality, so that the process may be compared to that of calcareous infiltration of lifeless organs in the midst of the organism. There is a similar tendency to the formation of calcareous deposits in the products of chronic inflammation of serous membranes, the pericardium, pleura, and peritoneum. These were formerly regarded as true bones. The muscular walls of the heart often show concretions of the same character. In chronic myocarditis all vascular granulations of whatever kind are subject to an infiltration of calcareous salts, such as occurs physiologically in the choroid plexus. The calcareous concretions, called phleboliths, formed in varices, arise also, probably, from ulterior changes in venous granulations. In old persons the tendons, and even the muscles around old fractures or near chronic arthritis, may often be infiltrated with calcareous salts to a greater or less extent. In fibrous tumours, in muscular tumours of the uterus, in chondromata, sarcomata, the walls of cysts, &c., either simple calcareous infiltration may be observed, or veritable petrifactions, which must, however, always be distinguished from true ossifications which may be met with, though rarely, under the same circumstances.

I. Infiltration of urates.—Urates in a solid form, either as granules or crystals, are only met with physiologically in the urine after cooling. In new-born infants amorphous urates are, however, often found in the straight tubuli of the kidney; they are coloured brick red by urinary pigment, and are visible to the naked eye in the form of small red lines. These deposits may be squeezed out of the straight tubuli by lateral pressure of the pyramids of Malpighi. Urates are thus deposited in the epithelial cells of the kidney and in the lumen of the uriniferous tubuli. Under the microscope urates appear either as very fine granules or as acicular crystals. Uric acid may be combined with magnesia or with lime, but generally it is in combination with soda. Urates are decomposed by even the feeblest acids, and the resulting uric

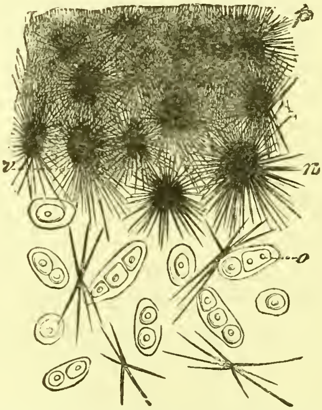

Fig. 41.—Section of an Articular Cartilage infiltrated with Urate of Soda in a Gouty Subject.

p, articular surface of the cartilage; *n*, acicular urates; *o*, cartilage capsules. Magnified 200 diameters.

acid, soluble in the nascent state, crystallises first in the rhombohedric form, but subsequently, as the uric acid crystals go on increasing, the two obtuse angles are cut off by parallel lines, and hexagonal lamellæ are formed; later very various forms are produced showing the molecular dissymmetry of uric acid.

Uric acid and urates, like the other salts which the urine normally and pathologically contains, may form concretions and constitute urinary calculi.

In gout, urates in the form of granules or crystals are deposited in the cartilages, bones, synovial membranes, tendons, skin, and kidneys. Everywhere the deposit is primarily made in the cells which are the centres whence the free crystals spring. These penetrate into the neighbouring ground substance, notwithstanding the resistance offered by the various tissues.

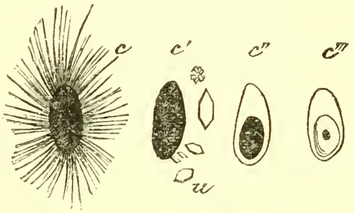

FIG. 42.—URATES DISSOLVED BY ACETIC ACID.

c, cartilage-cell and capsule bristling with acicular crystals; these crystals disappear the first; then in the figures c′, c″, c‴, the amorphous urates are gradually dissolved, whilst uric acid crystals are formed, u. Figure partly diagrammatic.

The primary appearance of uratic infiltration in the cells proves that the latter play an active part even in the phenomena of simple deposit, and differentiates this process from that of calcification, in which infiltration commences primarily in the ground substance.

J. Lesions caused by an excess of nutrition of the cells and tissues.—When nutritive materials reach the elements and tissues in great abundance, particularly in the case of irritation, the following phenomena are observed to take place in the cells: the nucleus, which in certain cases was atrophied and hardly visible, enlarges; the nucleolus becomes apparent; the protoplasm swells and absorbs plasma; the entire cell, which was long, flat, or very irregular, tends to become globular. This state differs from serous or albuminous infiltration of the elements, a lesion in some degree passive, in that the phenomena of excessive nutrition are characterised by an exaggerated activity of the cells, generally soon followed by their multiplication. Physiological examples of this hyper-nutrition of cells abound during development. It is thus that cartilage cells enlarge near the centres of ossification; that the muscle cells of the uterus and the muscular fasciculi of the heart hypertrophy during gestation; and that the epithelial cells of the mamma become greatly enlarged towards the end of pregnancy.

The most striking pathological examples of this hypertrophy of the elements from excess of nutrition are those drawn from facts observed in the connective tissue of adults. In the normal state extremely delicate flat cells may be observed in this tissue, but when subjected to pathological irritation they show a large nucleus as well as a granular and well-developed protoplasm. Every irritated cell, whether it belongs to cartilage, tendon, or epithelium, shows analogous phenomena. In hypertrophy of the muscles from excess of nutrition, as may be observed after excessive exercise, in hypertrophy of the heart, for example, most authors suppose that the muscular fasciculi are increased in volume. This supposition is very probable; but we may remark that nothing is more difficult than the appreciation of the diameter of a muscular fasciculus, which is composed of a soft and elastic substance, the contractions and elongations of which alter the diameter. According to the microscopic methods hitherto employed very varying results have been obtained.

Hypertrophy of the cells from excess of nutrition directly leads us to the study of their pathological multiplication, which will be next considered.

II.—Formative Lesions; New Formation of Cells.

Cells alone are capable of multiplication, the ground substance, which seems to be dependent on the cells, taking no direct part in this phenomenon. To Virchow is due the credit of having first demonstrated the importance of cell multiplication in pathological processes. Virchow distinguished two forms of pathological multiplication of cells. In the first the elements of new formation differ neither in their form nor in their function from the parent cells; this is simple **hyperplasia.** In the second the elements of new formation differ from the parent cells, and aid in the formation of a new tissue; this is what is called **heteroplasia.** Hyperplasia and heteroplasia,[1] which Virchow considered only from the pathological point of view, exist also in the physiological state, as we have already pointed out in speaking of ossification.

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[1] These names are ill chosen, in that they presuppose that the facts represented by them are only observed in pathology, whilst the phenomena of hyperplasia and

All cells do not seem to have the same aptitude for multiplication. A nerve cell has never been observed to multiply, nor has a muscle or a keratic cell, &c., whilst on the contrary, cells of the first group of tissues examined, those simply composed of protoplasm surrounding a nucleus, proliferate with the greatest facility. Embryonic cells or those recently developed are very prone to multiplication, whilst the process is no longer observed, or only in a very feeble degree, in cells which have reached their final form. Thus the white blood-corpuscles or lymph cells may be followed through all the phenomena of physiological cell multiplication, whilst it is very difficult to observe the proliferation of cells of the *rete mucosum* after birth.

In pathological hyperplasia cell multiplication always takes place in an uniform manner. The nucleus enlarges, the nucleolus becomes voluminous, constricted, and divides into two (fig. 6). The division of the nucleus may be effected by cleavage or by strangulation ; the nucleus then has the form of a wallet, biscuit, or hour-glass (fig. 6), &c. Each new-formed nucleus is surrounded by protoplasm, which is itself divided by cleavage or by constriction ; these modes of division may be met with one beside the other in the same element. Thus in the place of one cell there are two or a larger number of elements. Neither the secondary membranes of cells nor the ground substance of the tissue ever participate in these divisions ; they, on the contrary, more frequently soften and dissolve. The cells thus formed do not differ notably at the beginning from embryonic cells, but they soon take characteristic forms.

When a new cell tends to reconstitute the tissue in which it is developed, although it may pass through various phases, Virchow says that there is hyperplasia. If, on the contrary, it forms part of a tissue differing from the generating tissue there is heteroplasia. Thus when in cartilage a cell divides in the way we have described, the capsule remaining completely inert, there are at first two cells capable of secreting round themselves cartilage capsules ; but on the irritation becoming more active, instead of two cells a much greater number are formed, they are then no longer cartilage cells secreting capsules, but begin and remain as embryonic cells. At this stage of growth, if the irritation

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heteroplasia constitute on the contrary the physiological mode of formation of cells and tissues in the healthy organism.

cease, each new embryonic element becomes again a cartilage cell, surrounded by its own capsule. There is then in this succession of phenomena something more than simple hyperplasia, according to the meaning Virchow gives the word; there is veritable heteroplasia ending finally in hyperplasia. What we have just said of cartilage may be applied to connective and all other tissues, and shows the inanity of the words *hyperplasia* and *heteroplasia*. In osseous tissue the phenomena are still more striking. Under the influence of an intense formative irritation, the osseous trabeculæ are absorbed and a medullary embryonic tissue is produced in their place. This is a veritable heteroplasia. But when the irritation ceases this medullary tissue becomes again bone, and bone often much more compact, far richer in bone corpuscles, than the primary osseous tissue. According to Virchow there has been hyperplasia of the osseous tissue ; but this hyperplasia was succeeded by heteroplasia. It is evident from this example that these words are apt to give rise to confusion of ideas. They are only useful to recognise coarse and definite effects, for example, a formation of epithelial or fibrous tissue in bone ; but they will not bear examination when details, and the intimate mechanism of the evolution of products, are considered. We therefore employ the word hyperplasia only in the sense of cell multiplication.

The detailed description given in the first pages of this work of the methods of formation of embryonic cells dispenses us from returning to the subject ; the process of new pathological formation is, in fact, identical with that of physiological formation.

When a cell proliferates it gives origin to embryonic or indifferent cells. These, if the irritation ceases or is slow, return to their primitive state and reconstitute the generative tissue. If the irritation persists with intensity, the generative tissue is entirely destroyed ; the embryonic cells are then incapable of constituting a definite tissue and concur in the formation of pus, or become organised into a tissue deviating from the primitive type. In the case where irritation ends in the construction of a tissue differing from the generative tissue, embryonic cells undergo the same modifications as in the physiological development of each tissue. It is in this way that almost all tumours originate. We shall return to this subject when considering tumours.

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CHAPTER III.

INFLAMMATION.

I.—DEFINITION OF INFLAMMATION.

REDNESS, pain, heat, and swelling have, as the essential clinical characters, served from all antiquity to characterise inflammation. These primitive phenomena are followed by resolution, induration, suppuration, or gangrene.

Taken separately, none of these phenomena are peculiar to inflammation, for redness, pain, and heat may be caused by some transient nervous disturbance; tumefaction may be due to simple œdema; induration and tumefaction together also characterise tumours; gangrene may occur whenever blood-vessels are obstructed. Suppuration even is not constant in inflammation; it often exists without any of the other phenomena, and all the conditions of pus formation are so far from being elucidated that it is at present impossible to say if suppuration is invariably due to inflammation. It is true that in typical cases, where all these characters are found united, as in cellulitis, inflammation is well defined; but a good definition should comprise all inflammatory states. An attempt has been made to define inflammation by its supposed cause, hence the vascular theory which cannot, however, be applied to non-vascular tissues, and is therefore insufficient; hence, also, arose the hypotheses of the neurists and humourists, which are far from explaining all the facts observed in their entirety and order, particularly in tissues unprovided with nerves or vessels. Brown and Broussais, though they viewed the question from different points of view, considered inflammation to be an exaggeration of the physiological forces. According to Broussais, irritability, or the reaction shown by tissues when placed in contact with an irritant, is a property general to all living tissues. Irritants, which by their incessant action preserve life, are all either external or internal agents in contact with the tissues, and inflammation is nothing else than the result of an irritation more intense than normal. This hypothesis of Broussais has been strengthened by histological research. Virchow considers that irritation is developed by irritants existing in the cells as the essential condition of their own life. Cellular irritability is, according to him, functional, nutritive, or formative, but he avoids using the word inflammation. It is certain that inflammation, as seen clinically in its entirety, consists essentially in an excessive activity of nutrition and formation of anatomical elements. We do not propose entering into metaphysical discussions to which the words irritability and irritation may give rise—discussions which are most frequently based on a subtle and involved play on words—for we wish to occupy ourselves with observed facts. When an irritant is placed in contact with the tissues of a living animal (the thorn of Van Helmont), the same chain of symptoms is produced as occurs clinically in man in diseases called inflammatory, phenomena which we consider typical of simple inflammation. In the same way septic or specific inflammation is probably connected with the presence in the organism of microphytes and microzoa, which, acting like so many thorns, are alone sufficient by their presence to determine inflammation, but which are also more or less irritating in virtue of the various chemical substances they elaborate. The definition of inflammation and the study of its intimate phenomena rest, we consider, solely on experiment.

We define *inflammation* as *a series of phenomena observed in the tissues or organs, analogous to those produced artificially in the same parts by the action of a physical or chemical irritant.*

The different action of the agents of which we may avail ourselves in experiment, enables us to foretell the diversity of the modes of inflammation we have to study in human pathology. Induced inflammation serves best to modify the conditions under which the phenomena are produced, to study their various phases, and to observe during life, and immediately after death, the mode by which the products of inflammation are developed. In traumatic inflammation in man, even when the conditions are as well defined as in an experiment, it is generally impossible to study all the inflammatory lesions completely, for at the moment of examination cells have already undergone post-mortem changes, unless the inflamed parts have been surgically removed. Thus we shall begin our study by analysing inflammation artificially produced in animals, and shall consider the principal tissues, vascular and non-vascular.

II.—ARTIFICIAL INFLAMMATION OF NON-VASCULAR TISSUES.

If the permanent cartilages are taken as the subject of experiment, for example the costal or diarthrodal cartilages, and a part of the surface be exposed, at the end of a week it will be covered with a grey pulpy layer. If, now, a section be made through this pulpy layer and the cartilage which it covers, this is what is observed. In the layers of cartilage furthest removed from the wound, cartilage capsules are seen containing cells, the nuclei of which become visible by the action of a solution of picric acid (*a*, fig. 43). Passing from the distant layers towards the solution of continuity, the nuclei of the cells are seen to become larger, the protoplasm more abundant, and the capsules more voluminous. Soon this nutritive irritation is transformed into formative irritation, the nucleus divides, still being surrounded by a single mass of protoplasm, the latter divides in turn to furnish each of the new nuclei with a distinct mass. Each cell then secretes around itself cartilaginous material in the form of a capsule. Thus far the irritation has not modified the structure of the cartilage nor the property which its cells possess of secreting around themselves cartilaginous material. The zone (*c*, *d*, fig. 43), in which cartilaginous proliferation is observed, is more or less extensive. Further on, the surface of the cartilage is festooned, each depression corresponding to a cartilage capsule which has ruptured. Beside these are seen capsules still entire and filled with cells which have become embryonic, and lost the property of secreting cartilage around them. The grey surface covering the traumatic solution of continuity is embryonic tissue (*e*, fig. 43); here blood-vessels are developed (*i*, fig. 43) springing from the surrounding parts.

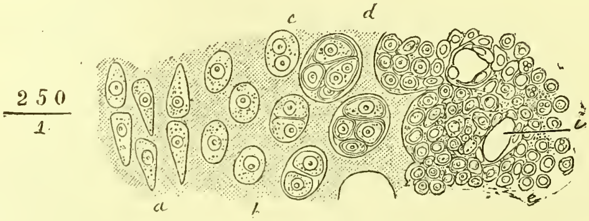

FIG. 43.—SECTION OF CARTILAGE ARTIFICIALLY IRRITATED.

a, capsules and cells of the deep layer of the cartilage; *b*, the same spherical; *c*, *d*, the same undergoing division and proliferation and forming an embryonic tissue; *i*, vessels from neighbouring parts. Magnified 250 diameters.

Embryonic tissue is produced from cartilage at the same time that the latter is destroyed.

Epithelia are also non-vascular tissues, though an investing epithelium generally lies on a membrane richly provided with blood-vessels. The great omentum is an exception to this rule. This large fold of the peritoneum is formed of a sac, the walls of which are not composed of a continuous fibrous membrane, but of a kind of network of unequal meshes, and of fibrous trabeculæ of very variable thickness. The thickest alone contain adipose cells and blood-vessels. The most delicate have no blood-vessels, and represent a single fasciculus of connective tissue, or two of these fasciculi intimately united. All these trabeculæ are covered by a single layer of large epithelial cells. The form and structure of these cells can only be appreciated by nitrate of silver staining. The silver is deposited between the cells and defines their outlines. They then appear as plates moulded exactly on the surface of the fibrous trabeculæ; in such preparations, afterwards stained with picrocarminate of ammonia, a nucleus is apparent.

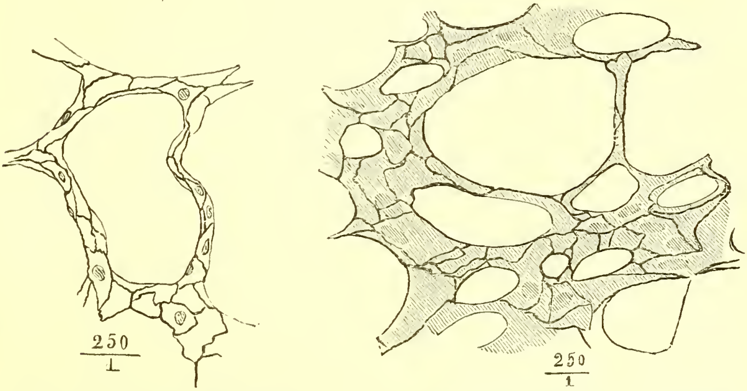

Fig. 44.—Great Omentum of the Rat stained with Nitrate of Silver. Normal condition.

This arrangement of the large omentum only exists in adult mammals; in the new-born it is composed of a continuous membrane. The observation should, therefore, be made on adults if it is desired to study the morbid changes which take place in the endothelium of the omental trabeculæ in consequence of irritation. This is excited by injecting a few drops of a one per cent. solution of nitrate of silver or tincture of iodine into the peritoneal cavity. Twenty-four hours after the operation the peritoneal fluid is cloudy and contains cells. Some of these resemble pus cells, others are larger and contain one or more ovoid nuclei, with well-defined borders, while between these two species of cells intermediate forms are observed.

By the nitrate of silver process it may be ascertained that endothelial plates are no longer present on the trabeculæ of the great omentum. On the trabeculæ, or between them, large globular cells, uninucleated or multinucleated, may be found (figs. 45 and 46). In these cells all the phenomena of cell multiplication can be observed. This multiplication is very active, and the hypertrophied cells make salient projections on the trabeculæ to which they adhere, sometimes by a large surface, sometimes merely by a single point. They may become detached and continue to exist and vegetate in an isolated state in the peritoneum. They have no cell wall, and are composed of a soft granular

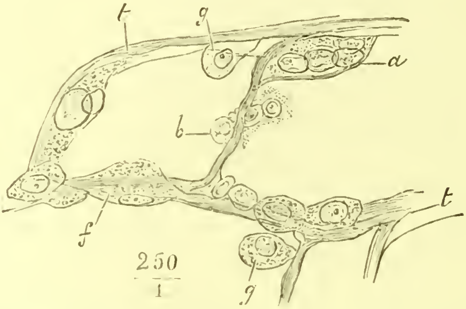

Fig. 45.—Great Omentum of the Rat artificially Inflamed and treated with Nitrate of Silver.

a, epithelial cell proliferating; *b*, pus-cell; *g*, *g*, epithelial cells which have become globular and prominent, separating themselves from the fibrous trabeculæ; *f*, tumefied epithelial cell, but still adherent to the trabeculæ. Magnified 250 diameters.

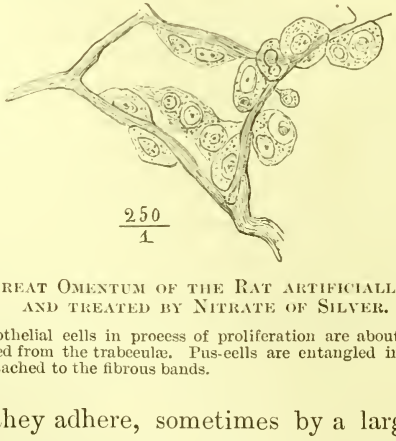

Fig. 46.—Great Omentum of the Rat artificially Inflamed and treated by Nitrate of Silver.

The endothelial cells in process of proliferation are about to become detached from the trabeculæ. Pus-cells are entangled in the fibrin and attached to the fibrous bands.

protoplasm, capable of taking the most varied forms and of sending out amœboid processes. The fibrinogen exuded from the vessels gives origin to filaments of fibrin which, surrounding the new cellular elements, may fix and maintain them for some time attached to the trabeculæ. Pus cells are the final product of this new formation. At the end of five or six days, islets of pus cells, or cells in process of development, may still be found; but the majority of the cells, now large and turgid, become reapplied against the surface of the trabeculæ still showing swollen projections; they diminish in size, flatten out against the trabeculæ, show a less granular protoplasm, and return to their primitive type (*a*, *b*, fig. 47). At the same time granular elements undergoing fatty degeneration are found in the peritoneal cavity. These are elements which, free in large numbers in the peritoneal cavity, are not placed under conditions favourable for nutrition. We have seen the same phenomena occur in pus cells which had penetrated a piece of pith placed within a serous cavity. Along the vessels of the vascular networks cells are found infiltrated with fat granules and also granular bodies.[1] These cells must be

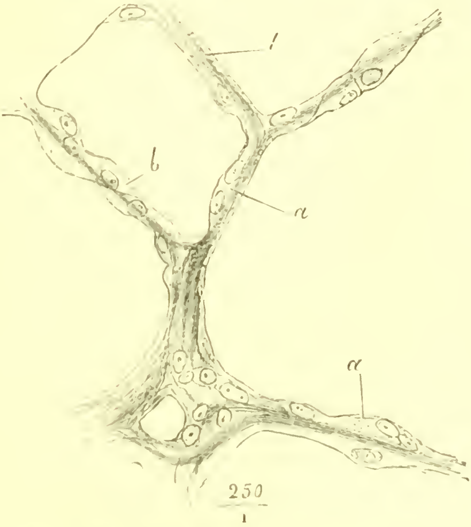

FIG. 47.—GREAT OMENTUM OF THE RAT A WEEK AFTER ARTIFICIAL IRRITATION.

The endothelial cells are seen at *a* to have become re-attached to the trabeculæ; their protoplasm is less granular than in the preceding figures, and they form at *b* an almost continuous investing membrane; at *a* the protoplasm is divided into distinct cells, which project, and are not flat and lamellar as in the normal condition.

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[1] Since the first edition of this manual was published many histologists have practised experiments consisting in introducing into the peritoneal cavity, or into

distinguished from those which, by reason of their amœboid property, absorb the fat in their vicinity. The fat does not then appear in extremely fine granules, but in large drops.

In concluding this subject we wish to point out that there are two opposite kinds of phenomena due to the inflammatory process; one consists in an exaggerated nutrition and a formative irritation of cells, the other in the fatty degeneration and death of the oldest cell elements. The former alone really belong to inflammation proper, the latter being explained by the fact that the cells are no longer placed under conditions favourable to life.

III.—EXPERIMENTAL IRRITATION OF VASCULAR TISSUES.

Osseous tissue may be taken as our example, for here phenomena are easily observed as they occur. The osseous trabeculæ limit spaces in which the medulla, an exceedingly active and vascular tissue, is the seat of almost every kind of nutritive and formative change, which may be observed in each medullary space in an isolated manner.

If in a rabbit, or some other small mammal, the bone is pierced and a thread introduced, inflammation is produced much more rapidly than in cartilage, and in two or three days it can be studied. A small portion of the irritated bone should be placed in a $\frac{1}{1000}$ solution of chromic acid, or in a concentrated solution

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the lymph sacs of the frog, or into the subcutaneous cellular tissue of mammals, foreign bodies into which lymph cells could penetrate. These foreign bodies were pith, as in our early experiments, or thin sheets of glass, the surfaces of which were so applied to each other that a flat capillary space was left between them. The advantage of tubes and lamels of glass over pith and every other opaque porous body is that, after being withdrawn from the body of the animal, the elements which had passed into or between them could then be studied under the microscope in the living state. If these foreign bodies be allowed to remain five or six days in a serous cavity or in the connective tissue, there are found, beside the ordinary lymph cells, other cells much larger, and containing one or more nuclei. The number of nuclei found in these cells is so great that they have been called giant cells. These experiments have been made by Ziegler, Heidenhain, Senftleben, etc. Hypertrophy of lymph cells often seems to result from the amœboid activity of these cells, as they absorb granules and minute bodies situated in their neighbourhood, or grains of vermilion or myelin if introduced into the serous cavity previous to the foreign body. Cohnheim even maintains that lymph cells may devour one another, so that a few considerably enlarged cells may be formed containing in their interior more or less ordinary lymph cells. But we are not of the opinion that a lymph cell can absorb other living cells; it is probable that amœboid absorption can only be exerted on cells which are dead or which have lost their amœboid activity.

of picric acid, and when softened, delicate sections should be cut, and the changes which have taken place studied. Let us take, for example, a short bone, or the extremity of a long bone. In the case of artificial irritation, such as we are now considering, there is at first a formation of embryonic tissue from the subperiosteal medullary cells and those contained in the medullary spaces. These medulla cells are not, in the normal state, inclosed in a solid ground substance, and can be easily isolated. Some are small, the *medulla* or *marrow cells* properly so called (*médullocelles*); others are large with one or more ovoid nuclei, *mother cells* (*myeloplaxes*). There are besides large fat cells, and fusiform or stellate cells. It is from these various sources that new embryonic cells develop.

In the fat vesicles of the irritated medulla, the nucleus hypertrophies and divides; the protoplasm, increased in quantity, surrounds each nucleus; at the same time the fat disappears and is replaced by an albuminoid fluid. The new elements multiply and end by completely filling the fat vesicle, the membrane of which is either destroyed or ruptured, and the embryonic cells are liberated. The medulla cells take on the characters of embryonic cells, which they resemble. The multinucleated cells, which were flattened and dried, become turgid, their nuclei multiply by division, and buds are given off from them, which on separation form free embryonic cells. If the irritation be continued, the osseous lamellæ, contiguous to the medullary tissue, are absorbed, and the bone cells (the bone corpuscles or lacunæ all contain cells) fall into the medullary space. It is thus that the medullary spaces increase in size, are filled with embryonic cells, and that the osseous trabeculæ undergo absorption (*vide* fig. 49).

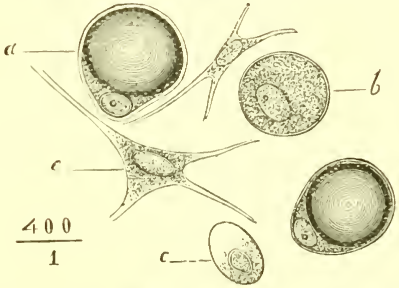

FIG. 48.—IRRITATED MEDULLA CELLS AND FAT VESICLES.

a, fat vesicle, the nucleus of which is hypertrophied and surrounded by protoplasm; *b*, fat vesicle, the fat of which has been absorbed. Magnified 400 diameters.

The intimate mechanism of this phenomenon will be studied in detail when considering osseous tissue.

At the same time the capillary blood-vessels undergo very important changes; the cells of which they are composed swell, their nuclei become more apparent, so that in transverse section the endothelial cells are seen to be turgid and very distinct. These swollen cells project into the lumen of the vessel and may impede the circulation (*vide* fig. 50, *v*).

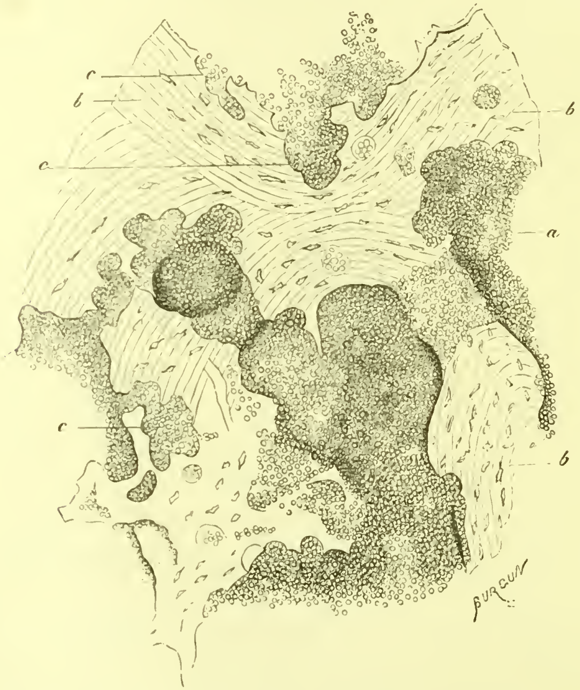

FIG. 49.—ACUTE SPONGY OSTITIS OR FUNGOID OSTITIS.

a, embryonic medullary tissue; the bony lamellæ *b*, are irregularly notched into festoons under the influence of the activity of the medullary tissue. The same has taken place at *c*. Preparation made from a bone decalcified by chromic acid. Magnified 100 diameters.

In subcutaneous cellular tissue, analogous phenomena take place as a consequence of artificial irritation. This tissue is composed of fat vesicles and flattened cells situated between bundles of connective-tissue fibres. The connective-tissue cells first hypertrophy, so that their nuclei, delicate and lenticular in the normal condition, become globular and of a diameter of 10 to 12 μ, and their protoplasm becomes granular and very visible (*e*, fig. 48). Soon, at the end of a few to 24 hours, their nuclei as well as their protoplasm divide, and in the place of one ordinary connective-tissue cell, two or more embryonic cells are present, and are arranged in elongated islets or in tracts between the fibres.

In fat cells the protoplasm becomes distinctly visible, the nucleus divides as in the medulla cells, the fat disappears (it is possible that the fat enters into new combinations, not discoverable by the microscope) and proliferation continuing, each fat vesicle becomes a little nest of embryonic cells (*c*, fig. 50). Proliferation of fat cells does not take place so rapidly as that of ordinary connective-tissue cells, and as moreover all the fat vesicles do not undergo change at the same time, they may be found long after the commencement of inflammation imprisoned in the midst of embryonic tissue.

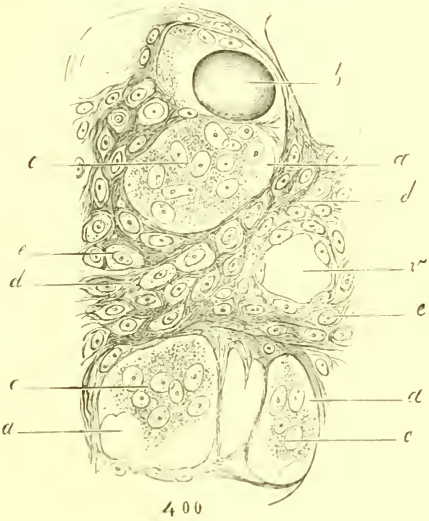

FIG. 50.—ADIPOSE TISSUE OF THE DOG FROM A DEEP WOUND UNDERGOING REPAIR.

a, *a*, spaces occupying the place of fat vesicles, the fat of which, *b*, has been absorbed, and filled by nuclei of new formation, *c*, surrounded by granular protoplasm; *e*, embryonic cells, *v*, section of a blood-vessel, the wall of which is composed of embryonic cells.

While the cells are the scene of the changes indicated above, the fibrous ground substance of the connective tissue absorbs serum, the fibrils become less defined and are finally absorbed and disappear. According to Rindfleisch they undergo mucoid change. Whatever it may be, their final change is into a soft substance. The embryonic cells, sprung from the connective-tissue and fat cells, become free in the midst of an amorphous mass; they are the more numerous as the foreign body or the solution of continuity is approached.

Elastic fibres undergo the same fate as that of the connective-tissue fibres and the secondary membranes of the fat cells; they break up into fine molecules which in turn completely disappear. The blood-vessels have exactly the same appearance as that described in the bone medulla; the flat and resisting cells of the capillary walls become turgid and soft, and there is an evident multiplication of their nuclei.

In batrachians the results of experimental inflammation are the same as those just described. Thus in the frog, if a foreign body be placed under the skin in the dorsal lymph sac, a gelatinous tissue is produced around it, feebly adherent to the wall of the sac, and to the nervo-vascular filaments which cross it. This tissue is formed of cellular elements endowed with amœboid movements, immersed in a ground substance small in quantity and soft. This gives it its gelatinous consistency. If this tissue be immersed in a ·3 per 100 solution of nitrate of silver, until the surface is stained, and the stained layer be then removed by a razor, preparations are obtained in which the ground substance, stained by the nitrate of silver, is seen to define the limits of stellate or fusiform spaces joined together by broad and short anastomotic processes. If a morsel of elder-pith be the foreign body placed under the skin, it will be observed that some of the cellular elements penetrate into the cells of the pith by the porous canals, and that many of them, having there lost their vitality, become filled with fat granules.

The various inflammatory phenomena which we have just described are the more important, as they occur in non-vascular as well as in vascular tissues; nevertheless the circulation has for a long time been recognised as playing a preponderating part in inflammation—a part which Cohnheim has by recent experiments reasserted, adding facts to which attention had not been sufficiently drawn.

Kaltenbrünner and Wharton Jones had studied the phenomena produced by irritation in the interdigital membrane and tongue of the frog and in the wings of bats; parts which, on account of their transparency, lend themselves to the histological study of the changes which take place in blood-vessels, after mechanical or chemical irritation. These authors made no distinction between capillaries and arteries or veins of small calibre, and included in one description all that occurs in these different classes of blood-vessels. They observed that the small blood-vessels first contracted, then became relaxed. With a very strong irritant the relaxation was almost immediate. Stasis succeeded. Contraction, then relaxation of the blood-vessels, and finally blood stasis, these were the facts established by their observations. This is simply the commencement of inflammation. Cohnheim's experiments are much more decisive. They led him to explain suppuration by the passage of the white blood-corpuscles through the walls of the blood-vessels. The migration of leucocytes in connective tissue, and particularly in the lacunæ of the cornea, was already perfectly well known. Recklinghausen had established this fact in the clearest manner, and suppuration had been already explained by him as the result of the migration of lymph cells. Waller had also observed the migration of white blood-corpuscles through the walls of the vessels, but these observations had not attracted sufficient attention, and it is in fact Cohnheim who has the honour of having formally settled the question.

Diapedesis is best observed in the mesentery of the frog. The animal having been rendered completely immobile by the injection of two drops of a ·1 per 100 solution of curare, the abdominal wall is opened on one side, the intestine drawn out by a pair of forceps, and the mesentery placed on a slide specially prepared.[1] In the mesentery thus spread out, the circulation may be studied in the capillaries, veins and arteries. In the arterioles the blood circulates rapidly in passing from the heart, and cardiac pulsations are still visible. In the veins the blood current is continuous, and is in the contrary direction. In the capillaries the course of the blood is very irregular; it stops, then continues, and sometimes runs back in the opposite direction, even in the same capillary. In curarised frogs the circulation is so active that, at the beginning of the experiment, the red corpuscles pass so rapidly that it is difficult to distinguish them. In contact with the internal wall of the blood-vessels, some red corpuscles and a great number of white are seen to slacken speed, while many of the white corpuscles are quite immobile. This immobility of the white corpuscles along the wall of the vessel, and which Poiseuille ascribed to the existence of an adhesive

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[1] The slide is formed of a flat piece of cork with a round hole in the centre. The frog is placed on its back on this piece of cork. Round the borders of this circular opening a ring of cork is fixed by pins. This ring should correspond in height to the size of the frog. The intestinal loop is then attached to the edge of the cork ring, so that the mesentery is spread over the circular opening. (Vide *Traité technique d'histologie*, p. 604.) [This observation can equally well, and should always, be made after pithing of the frog, thus avoiding all suffering to the animal.—Tr.]

MANCHESTER MEDICAL

layer, may be well observed two or three hours after the commencement of the experiment; this is owing to the fact that the white corpuscles change shape and throw out amœboid processes, by means of which they fix themselves to the vascular wall. Their irritability is greater the longer the experiment continues and the mesentery is in contact with the air. The corpuscles placed along the vascular wall are pressed against it by the blood current and become adherent. Sometimes the force of the current detaches a few of them, and when free they are seen to have the shape of a grenade, or the side which was in contact with the vascular wall has a bristly appearance, the rest of the surface being smooth. The little amœboid processes are withdrawn when the white corpuscles re-enter the circulation. But many of the corpuscles, in the small veins as well as in the capillaries, insinuate themselves into the vascular coats and traverse them, passing into the connective tissue or a lymphatic sheath, or become free on the surface of a serous membrane. Some hours after the commencement of the experiment, the various phases of diapedesis of white blood-corpuscles may be observed. On directing attention to the optical section of a vessel, a number of corpuscles of different sizes are seen to protrude into the lumen, some pyriform in shape are attached to the wall by a slight pedicle, others are adherent by a large surface and are hemispherical. The latter should be specially examined in studying the process of migration. The part which projects into the interior of the vessel, while retaining its rounded shape, progressively diminishes in size until a simple brilliant spot is left. Finally this point disappears, and at the same time outside the vessel a little irregularly shaped mass appears and increases in size; various processes are sent out which extend from the external surface of the vessel into the connective tissue. The intravascular portion of the migrating corpuscle is regular and spherical, its external portion being amœboid.

In order to more easily follow the migration of leucocytes it is useful to colour them, as Cohnheim did, by means of finely pulverised substances, anilin blue, for example, dissolved in alcohol and precipitated by water. This substance is injected into the dorsal lymph sac of the frog. When a white corpuscle has absorbed into its interior coloured particles, and is afterwards found attached to the wall of a vessel and traversing it, its movements, owing to the coloured particles it contains, can be easily followed.

When the white corpuscles have passed through the coats of the walls of a small vein or capillary, the channel they have created remains patent for a certain time. It is impossible to recognise these channels in mesenteric vessels whilst the circulation is pursuing its course. But if the vessels which have been the seat of an abundant diapedesis are afterwards stained with nitrate of silver, the walls show numerous openings between the endothelial cells. These openings are known under the name of *stomata*.

These facts being understood, it is easily perceived how diapedesis of white corpuscles may be accompanied by that of the red. There is not here an active migration but a passive transportation of red corpuscles. When a red corpuscle passes into a stoma it elongates, and when it reaches the outer surface it is of an hour-glass shape, the strangulated part being at the point of the vascular wall, while the two swollen halves are seen to be one within and the other without the vessel. All these phenomena are caused by the lateral pressure of the blood current ; not unfrequently the red blood-corpuscles may be torn and broken up into round granules which can be recognised by their refraction and their special colour. Diapedesis of red corpuscles may be observed as easily as that of the white, and Stricker observed it before Cohnheim. It explains why red corpuscles are always met with in the products of inflammation.

Diapedesis of white and red corpuscles should not be looked upon as appertaining solely to inflammation. It takes place in the physiological state as may be observed in the interdigital membrane of the frog when not submitted to any irritating influence. The presence of white corpuscles in the meshes of connective tissue is owing to diapedesis, and also the presence of red corpuscles in any considerable quantity in lymph, for example, that contained in the thoracic canal. Diapedesis of the white corpuscles being thus a physiological phenomenon, it cannot of itself alone characterise inflammation as Cohnheim at first maintained. But inflammation is not a specific phenomenon ; it should be considered, as we have already said, as an exaggeration of physiological phenomena, exaggeration of the nutrition and formation of cellular elements and of diapedesis. The latter is little characteristic of inflammation, for inflammation occurs in tissues containing no blood-vessels for example, in cartilage, investing endothelium and the cornea, and among these tissues there are even some, such as cartilage, in which the migration of cells is impossible.

In the cornea, the cloudiness and suppuration which occur consequent on inflammation artificially produced by means of a wound or cauterisation with nitrate of silver, are explained by the migration of cells. Recklinghausen worked out this fact in an important research quoted above. In the physiological state, the cornea contains, besides the flat cells which are fixed and interposed between the fibrillar elements, a variable number of lymph cells, which wander among the interstices of the membrane. In the frog twenty-four or forty-eight hours after cauterisation with a pencil of nitrate of silver, the number of migratory cells may be observed to be considerably increased. Now Cohnheim asserts that all these migratory cells come from the blood, and in proof of this opinion he gives the following experiment. If, after injecting insoluble anilin blue into the lymph sacs of the frog, and after its absorption by the white blood-corpuscles, the cornea be artificially inflamed, the presence of white blood-corpuscles charged with anilin blue may be ascertained in this tissue. But it is easy to see, as we have established, that in experimental inflammation of the cornea there is proliferation of the fixed cells, and that these may then acquire properties similar to those of lymph cells.

To recapitulate, the lymph cells or pus cells which infiltrate the inflamed cornea are for the most part, as Cohnheim maintains, migratory cells from the blood, but to these must be added young cells due to proliferation of the connective-tissue cells of the membrane itself.

Influenced by his beautiful discovery Cohnheim thought to explain all inflammation by diapedesis, but while rendering him full justice, we must not lose sight of the important part played by cell activity and proliferation in the phenomena of inflammation.

IV.—Analytical Study of Inflammation.

Inflammation presents for consideration—1, hyperæmia or inflammatory congestion; 2, exudation; 3, new formation; 4, inflammatory degeneration.

1.—HYPERÆMIA OR INFLAMMATORY CONGESTION.

When hyperæmia has not existed long, it disappears after death, leaving no trace. Erythema gives place to cadaveric anæmia. After death the arterioles and small blood-vessels furnished with contractile coats undergo *rigor mortis*, and expel their contents into the large veins generally more deeply situated, so that the redness due to their repletion completely disappears. But if the hyperæmia has been intense, or long continued, the capillaries remain full after death. Hasse and Kölliker have noted this condition after chronic catarrh of the mucous membrane ; Lebert also noticed the persistent dilatation of capillaries in articular serous membranes affected with rheumatic arthritis. All anatomo-pathologists have since verified these facts in various organs. The blood-vessels are regularly distended in a cylindrical form, or from point to point in a fusiform or ampullar shape. Inflammatory redness has been explained by distension of vessels. This opinion is that generally adopted at the present time. Lebert has however remarked that some of the colouring matter of the blood may be diffused into contiguous parts. MM. Estor and Saint-Pierre (of Montpellier) have made some interesting researches on this subject of inflammatory redness. They find that the veins issuing from inflamed parts contain more oxygen than normally. They hence conclude that the red colour of inflamed parts is due to the fact that they contain a larger quantity of oxygenated blood. This is a new fact added to those already known, but which does not disprove the easily ascertained fact that in inflamed parts there is a larger quantity of blood, and that there is also extravasation of the red corpuscles and colouring matter of the blood, the presence of which may be recognised by the microscope in the tissues contiguous to the vessels. The epithelial and connective-tissue cells are often first yellow or reddish in colour and present pigment granules which become darker. This is one of the causes of the slate-coloured staining of certain cicatrices. Such is also the origin of pigmentation of the cells in chronic bronchial catarrh.

2.—INFLAMMATORY EXUDATION.

A. **Serous exudation.**—The existence of fluid exudations, effused from vessels and simply containing dissolved albumen, has been hitherto rather admitted than clinically demonstrated. Actually these fluids contain almost always variable quantities of fibrinogen, fibrin or mucus according to the parts affected.

B **Mucous exudation.**—This is met with wherever mucin is produced normally, especially on the surface of mucous membranes and in articular cavities. It contains coagulated filaments of mucin which do not disappear when acted upon by acetic acid, though this reagent throws down a granular precipitate. Mucin is deposited in filaments and forms thick layers on the articular surface of cartilage, notably in the case of white swelling. In acute articular rheumatism fibrin and cellular elements are present in addition.

C. **Fibrinous exudation.**—Fibrin does not escape from the blood-vessels in a coagulated state. Denys de Commercy holds that fibrin exists previously in the blood in a soluble state, and in exudations in the state of dissolved plasmin, and that this plasmin gives rise to fibrin by a process of duplication. Alexander Schmidt expressed a similar idea in different terms. According to him, there is primarily a substance called *fibrinogen*, held in solution, but which has the property of coagulating on combination with another albuminoid substance called *fibrino-plastin*. The globulin contained in the red blood-corpuscles is a fibrino-plastic substance, but the tissues, and the cells in particular, contain it, and may consequently be the agents of the coagulation of fibrinogenic substances. Schmidt has, however, altered his first theory, and now admits that to produce fibrin, not only a fibrinogenic and fibrinoplastic substance are required, but also the action of a ferment. This, which may be accidentally found in the blood contained in the vessels, is constantly deposited by the blood when in contact with the air. Under the influence of intense inflammatory congestion, fibrinogen escapes from the vessels and, combining with fibrino-plastin derived from the cells, fibrin is produced. Coagulation does not take place suddenly, it is successive, the exudation

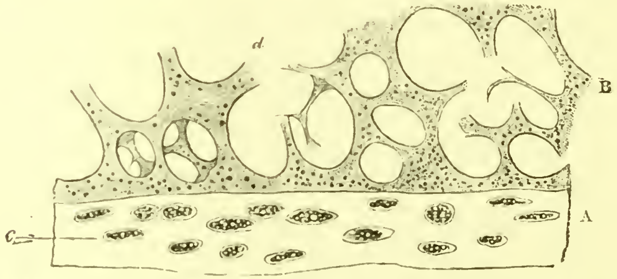

FIG. 51.—MUCOUS EXUDATION ON THE SURFACE OF AN ARTICULAR CARTILAGE.

From a case of White Swelling. A. Section of the articular cartilage showing cartilage cells, which are at the surface seen to be filled with fat granules. B. Mucous exudation composed of fibrils of coagulated mucin, *d*.

in contact with the neighbouring tissues alone undergoing coagulation. Thus in very abundant effusion into closed cavities, for example in the case of pleurisy with large effusion, there may be scarcely any coagulated fibrin. If the fluid from thoracentesis be collected, though absolutely serous at first, it soon begins to coagulate, owing to the penetration of particles present in the atmosphere which act as ferments. Fibrinous exudations have a limited existence owing to the changes fibrin always undergoes if it remains in the body. Whether disposed in filaments or in membranous lamellæ, it soon undergoes change from the fibrillar to the granular condition, and finally breaks down into complete molecular disintegration. It has nowhere been shown that fibrin can acquire a more advanced organisation. John Hunter put forth the hypothesis of the definite organisation of fluid emanating from the blood, or plastic lymph. Since then, the facts have been better studied, names have been changed and repeated, according to the first impulse given by Hunter that fibrin may become organised, but it has never been positively demonstrated. If fibrin becomes organised, it is under conditions and according to methods which have not yet been sufficiently studied to take a place in science.

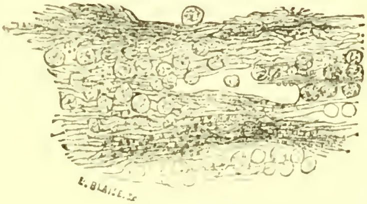

FIG. 52.—TRANSVERSE SECTION OF A PLEURITIC EXUDATION IN WHICH FILAMENTS OF FIBRIN AND PUS CELLS ARE SEEN.

Magnified 250 diameters.

D. **Hæmorrhagic exudation.**—In every inflammation, even in the most simple, in coryza for example, blood-corpuscles escape from the vessels and mix with the effused fluid; sometimes the amount is considerable, at other times it is hardly appreciable with the most attentive microscopic examination. In diffuse cellulitis red blood-corpuscles are always found mixed with pus cells at the commencement of inflammation. (We have indicated above the process by which red blood-corpuscles escape from the vessels.) Their presence in greater or less numbers tints the effused fluid more or less. The corpuscles break down and are absorbed by the lymph cells in their neighbourhood. Inflammatory degeneration will be studied later on.

E. Exudation composed of coagulated fibrin and mucin and containing cellular elements (the *croupous* exudation of German authors).—The term 'croupous exudation' has been used by German authors to signify an exudation which coagulates on diseased surfaces in the form of a membrane. This exudation is composed of cellular elements, differing according to the parts attacked, but always contains filaments of fibrin and sometimes mucin including pus cells. The filaments interlace and form a network, in the meshes of which cellular elements, epithelial and pus cells are retained, exactly in the same way as red blood-corpuscles are entangled by coagulated fibrin in a blood clot. This exudation is specially met with in inflammation of serous membranes and in acute pneumonia. German authors confound this fibrinous exudation with the false membrane of true croup, or the 'pseudo-diphtheritic' membrane of French authors.

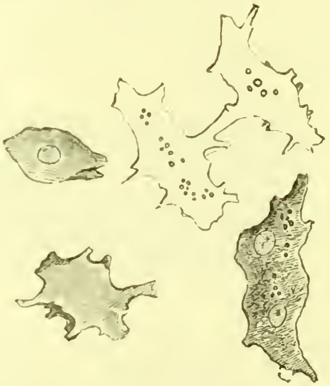

FIG. 58.—ALTERED EPITHELIAL CELLS FROM A DIPHTHERITIC FALSE MEMBRANE.

F. Diphtheritic false membrane and exudation.—Whilst fibrinous exudation persists after death, the false membrane of true croup has, on the contrary, almost completely disappeared by the time the autopsy is made, or it constitutes simply a pultaceous layer very different from that which is observed during life. According to E. Wagner these false membranes are not composed of fibrin, but of epithelial cells closely united yet capable of dissociation. On dissociating the membranes, Wagner has been able to resolve them into angular or refractile blocks, or into ramifying elements entangled together. He describes the numerous processes of these elements, which he compares to the antlers of a stag, and recognises intermediate forms between them and epithelial cells. In attaining such bizarre forms the cells become infiltrated with an albuminoid substance, lose their nuclei little by little, become transformed into homogeneous masses, and give origin to numerous ramifications. Wagner admits a fibrinous degeneration of these cells, although the presence of fibrin is not established in a positive manner. The diseased epithelial cells, changed into homogeneous blocks with ramifying processes, form in the pharynx whitish, thick, opaque layers of a fibrinous appearance, beneath which pus cells and hæmorrhagic exudations are often found. It is the latter which form the reddish ecchymotic islets noticed in the deep layer of these false membranes. In the larynx there are always many superimposed layers of these epithelial membranes and pus cells. We have verified the exactness of the description given by Wagner, and we have dissociated and coloured these cells by means of picro-carminate of ammonia; owing to the facility with which they are stained with carmine, we may conclude that they are not infiltrated with fibrin but rather with colloid matter.[1] The exudation of true croup is detached and thrown off as pus cells, while new epithelial cells are formed beneath it.

3.—INFLAMMATORY NEW FORMATION.

Under the influence of slight irritation, simple hyperplasia of cellular elements is observed, that is to say, the old cells give origin to new cells which preserve the characters of their progenitors; this idea is exactly represented by the word hyperplasia. If inflammation is more intense the old tissue is destroyed and is transformed into an embryonic tissue; there is then no longer hyperplasia, but inflammatory heteroplasia.[2] Human pathological anatomy agrees exactly with that we have learnt from the experimental study of inflammation. The process takes place in the following order: *Hypertrophy of the nucleus, division of the nucleus, increase then division of the protoplasm, destruction of the fibres or the ground substance, formation of embryonic tissue, formation of new vessels.* We will not here reconsider all these facts, but will only treat in detail of suppuration, the new formation of blood-vessels, granulation, cicatrisation, and the degenerations consecutive to inflammation. Degeneration occurs when embryonic tissue proliferates with great activity and cells multiply and accumulate without a simultaneous formation of new blood-vessels.

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[1] In diphtheritic false membranes the presence of bacteria, vibriones and spores of the micrococcus have been noted, and a special value attributed to them. It is possible that there is a microphyte or microzoon special to diphtheritis, but as those met with in false membranes may be found in the physiological state in the tartar of the teeth, the papillæ of the tongue, the crypts of the tonsils, it is well, we think, to exercise a wise reserve and wait for fresh observations before deciding the question.

[2] As an example of inflammatory heteroplasia there is none more striking than that of granulation tissue, which has the same constitution, whatever may be the tissue from which it springs, skin, synovial membranes, bone, &c. Bichat, who considered that granulation tissue was essentially formed of cellular tissue, and who compared the tissues of the body to the simple bodies of chemistry, could not conceive how granulations could spring from osseous tissue, though even he admitted the presence of cellular tissue in bone.

A. **Suppuration. Pus cells.**—Lymph cells so closely resemble embryonic cells that it is impossible to distinguish one from the other. When alive and capable of amœboid movements the irregular form of the nuclei is in relation with the pressure exercised by the protoplasm. In a state of repose or death they contain one round or oval nucleus, rarely two. Normally, a well-nourished cell gives birth regularly to two cells similar to itself, and even when hyperplasia is active multinucleated cells do not exist in great numbers. But if the supply of nutrition is cut off, the nuclei continue to divide without division of the cells, and cells may be seen to contain 2, 3, 4, or 5 small nuclei. These are then true pus cells, differing from embryonic cells only in the number and the size of their nuclei. In pus recently formed, whatever may be its origin, cells containing only one nucleus are constantly found side by side with multinucleated cells. Pus cells are then nothing else than embryonic cells, the vitality of which has diminished, if they have not completely ceased to live. Atrophy of the nucleus is constant in all elements which die or are eliminated, for example in the horny layer of the epidermis. Pus corpuscles may exist in large numbers in a tissue without their presence being revealed to the naked eye by the physical appearances of pus. Thus, they are contained normally in greater

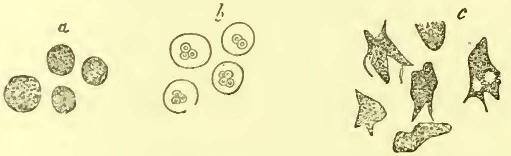

Fig. 54.—Pus Cells.

a, as seen in a neutral fluid; *b*, as seen after the action of water and acetic acid; *c*, living cells showing amœboid movements.

or less numbers in granulation tissue and in mucus and serous secretions; in thick or creamy pus there are a great number of pus cells, while serous pus contains fewer. The puriform appearance of a liquid is owing to the fact that it holds suspended a large number of small, solid, free corpuscles. Thus cream is opaque like pus because it holds in suspension many fat corpuscles; the puriform fluid of the Fallopian tubes, the renal papillæ and the intestinal mucus after death may contain only epithelial cells and yet perfectly resemble pus.

The physical and chemical characters of pus cells are as follows: they have no cell wall and are only composed of a mass of protoplasm and nuclei. In the fresh state and in the fluid in which they are bathed, they appear as finely granular masses irregular in outline, often with amœboid processes. The nuclei cannot always be seen, but on adding water they swell, from 8 to 9 μ, which is their normal diameter, to 11 or 12 μ; they become spherical and show easily, especially after staining with carmine, 2, 3, 4, or 5 nuclei of 2 to 3 μ in diameter. The nuclei resist the action of acetic acid, though under its influence the cell becomes spherical and paler, still bordered however by a very delicate line which finally disappears. Pus corpuscles do not differ, as we have already pointed out, from certain white blood-corpuscles.

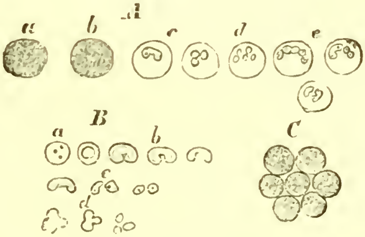

FIG. 55.—PUS CELLS.

A. *a*, *b*, in water; *c*, *d*, *e*, after the addition of acetic acid. *B*, division of the nucleus. Figure borrowed from Virchow.

The theory of pus formation.—According to an old opinion of Zimmermann, and the experiment just cited of Waller, it was believed that pus escaped direct from the blood-vessels. Cohnheim asserted the same, and lent this opinion the support of the experiments already described. But is pus always found thus? We are in the position to assert the contrary. The epithelial cells of all serous and mucous membranes swell and hypertrophy when irritated and their protoplasm becomes more abundant; they show all the different phases of multiplication by division; each one of the new cells may divide in turn, and when, in the smallest cells the nucleus divides without the cell participating in the division, pus cells are produced. Large mother-cells may contain a certain number of embryonic cells which very little will convert into pus cells. This is what is observed in pustules of the skin, in pemphigus, and catarrhal inflammation of the mucous membranes. Thus we admit two modes of pus formation: 1, by proliferation of cellular elements; 2, by diapedesis of white blood-corpuscles. In very rapid suppuration diapedesis is the most important factor.

Pus undergoes change very easily; according to its age and the influence of the substances with which it is in contact it undergoes the following modifications:—

Fatty degeneration of pus cells occurs whenever pus becomes old. Inside the cells fine refractile fatty granules are formed, and are seen without the addition of water. Acetic acid does not act upon them. The presence of fat granules in the interior of pus cells is owing to two causes: the death of the cell and the active absorption of fat granules situated in its neighbourhood.[1] When pus cells are filled with fat granules they increase in size and reach 15 to 20 μ. They have been long known under the name of inflammation corpuscles, or the *corpuscles of Gluge*. These corpuscles seem to be peculiarly formed lymph cells which have absorbed fat granules near them. They generally have one, rather large, oval nucleus. They are more particularly found in the lymph spaces and in the lymphatic vessels leading from organs rich in fatty matter and which are undergoing a process of degeneration, the brain for example. Thus, the perivascular sheaths of the brain or spinal cord contain a large number of these corpuscles in the neighbourhood of a hæmorrhagic focus or a centre of softening. A fact which proves that it is by penetration that the fat finds its way into the cells, is that red blood-corpuscles or fragments of them, or blood pigments, are found in the same elements. As to the fatty degeneration of pus cells connected with the death of the cells, this is chiefly met with in large purulent collections. The corpuscles which are the seat of this degeneration contain only a limited number of small fat granules.

Caseous degeneration of pus cells is also observed when pus has remained a long time in an abscess or natural cavity. The serous part of the inflammatory product is absorbed, and the cellular elements pressed together, become angular and atrophied, and some present very fine fat granules, not modified by water or acetic acid. They form, by their conglomeration, a white or yellow caseous mass more or less dry. Such is one of the modes of origin of the angular corpuscles which Lebert looked upon as characteristic of tubercle. Pigmentary infiltration occurs in pus cells whenever a notable transudation of red blood-corpuscles accompanies suppuration. Calcareous transformation is produced in very old purulent foci. In gouty abscesses formed in the neighbourhood of small joints, acicular crystals of urate of soda are often found. Watery and acid transformation of pus is observed in bone abscesses. The pus in fact then contains lactic acid, under the influence of which the pus cells swell, their protoplasm dissolves, and their nuclei are set free. It is this serous appearance, well known to surgeons, by which they recognise chronic bone abscess at first sight. Pus cells are in time dissolved in the same way if the fluid contains a large proportion of water.

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[1] See p. 91, note 1.

B. **New formation of vessels in inflammation.**—Whenever inflammation occurs in a vascular tissue, tho blood-vessels undergo changes which often result in the formation of new vascular branches. This inflammatory new formation of vessels is analogous to that which takes place in tumours and is the more interesting to study as its mode of production is more common. The capillaries are, as we know, formed of nucleated endothelial cells cemented together at their edges. When irritated, these cells swell and soften, and if the inflammation continues, their nuclei multiply by division. These phenomena are identical with those already described in the endothelial cells of the great omentum in artificially produced peritonitis. The blood-vessels of the inflamed tissues return to the embryonic condition, that is to say, they are formed of embryonic cells arranged in rows, and having in their centre a canal through which the blood circulates (fig. 50 v. p. 95). This modified wall of the vessel is soft and is easily distended or ruptured by the blood pressure. It is clearly understood how, under such conditions, the passage of red and white blood-corpuscles through the walls of the vessel is rendered easy. This inflammatory change in the walls of blood-vessels, which we indicated in the first edition of this manual, has been re-studied by many histologists. We wish to notice among these the thesis of our much-regretted friend Chalvet, in which the view that diapedesis in inflammation is allied to a change in the vascular walls was first expounded. This view has been recently developed by Cohnheim. The capillaries and small blood-vessels thus modified become the point of departure for new vessels in various ways; sometimes a capillary loop enlarges and makes a long parabolic curve, sometimes prolongations spring from the convex portion of a capillary loop and become hollowed in proportion as the blood penetrates. According to Rindfleisch the cells contained in the exudations of serous membranes become elongated and disposed in parallel rows, between which the blood penetrates from a neighbouring capillary; but it is very improbable that the new formation of vessels occurs in this manner. Finally, as Meyer and Plattner have shown, in embryonic tissue the capillaries may be seen to start from plasmatic cells according to the process described by Kölliker in the membranous expansion of the tail of the tadpole. These cells have anastomosing canalicular processes which put them in relation with the old vessels, after which they enlarge so as to receive the blood-corpuscles.

It is well known that inflammatory new membranes which rapidly develop on the surface of serous membranes, notably on the pleura in acute pleurisy, are soon provided with blood-vessels, the abundance of which is not exceeded by any other vascular organ. This exuberant development of capillaries, which takes place in a few days' time, can hardly be explained by simple expansion of the few vessels belonging properly to the normal pleura. An independent new formation must therefore be admitted. Some authors had formerly expressed the opinion that it must be so, but no direct proof had been adduced in support of this view, which was for a long time abandoned. No micrographic anatomist had ever supported it. It wanted a basis borrowed from normal histology, for vaso-formative cells were yet unknown.

Vaso-formative cells.—These cells can be easily observed in the omentum of young rabbits.[1] They appear in certain milky spots which are not yet connected with the blood-vessels of the omentum. These spots are characterised by a group of lymph cells in the midst of which the vaso-formative cells are situated; originally they do not differ much from lymph cells, but they soon increase in size, and in the midst of their protoplasm red blood-corpuscles are formed just as in the midst of vegetable cells starch granules appear. They then send out processes which ramify and anastomose with one another, whilst the formation of red corpuscles goes on within them with increasing activity. They soon cover with their ramifications the whole extent of the milky spot, forming a network, at the nodal points of which red corpuscles are found accumulated, while at others anastomatic branches are given off. It is only later that the small arteries and veins, springing from the principal vessels of the membrane, become connected with the vaso-formative network and a circulation is established, by means of which the red corpuscles, *formed in situ*, are carried into the general current. It may sometimes happen that by a freak of nature no veins are connected with the capillary network of a milky spot, the connection being only with the arterial system. A network may then be produced along the course of a small artery.

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[1] For fuller information consult Ranvier's *Traité technique d'histologie*, p. 625.

It is from the arteries and veins of the great omentum that the capillary arteries and veins spring and are pushed forward till united with the newly formed capillary network of a milky spot. The method of growth of these vessels is according to a type well described by Golubew in his ‘Study of the Formation of Blood-vessels in the Membranous Expansion of the Tail of the Tadpole.’ He observed that in this membranous expansion the formation of blood-vessels takes place solely by the extension of old vessels, and not by connective-tissue cells, as Kölliker had affirmed. It was moreover already known that these cells are not hollow and cannot therefore form vessels by simple distension of their cavity. Vessels in the act of growing terminate by buds from which protoplasmic filaments spring, these thicken, elongate and anastomose with similar filaments springing from neighbouring vessels. They eventually become tubular. Arterioles directed towards the milky spots also terminate like the blood-vessels of the tail of the tadpole in protoplasmic filaments, and on reaching and joining the vaso-formative network they become tubular and establish a communication with the general circulatory system.

Although a sufficient number of observations on the formation of blood-vessels in inflammatory false membranes has not yet been made, it is probable that they develop in a manner similar to that described above, and that perfect capillary networks are formed independently in the exudations, so rich in lymph cells, of which at the beginning these membranes are composed. The old blood-vessels of the serous membrane finally communicate with the newly formed vascular network. The large multinucleated mother-cells, observed by Langhans a long time ago in serous exudations, were probably only vaso-formative cells.

C. **Granulations (granulation tissue)**, which by their fusion form membranes called pyogenic, are only developed on the surface of wounds, or inflamed surfaces communicating with the external air.

It is a general physiological law that in all higher animals the external, and part of the internal covering, especially at orifices where skin and mucous membrane meet, present papillæ; these are nothing else than permanent granulations. In the same way every new pathological formation on a surface takes this papillary or granulating form; for example, almost all tumours of whatever nature situated on the skin, or at one of the external orifices, assume this character. The granulation tissue of inflammation consists of embryonic tissue; it forms slowly in induced irritation, because, for its production, a large quantity of embryonic tissue and new blood-vessels are necessary. It gives the key to the process of cicatrisation of wounds, and histology teaches the cause of the different appearances of granulation tissue, differences well known to the surgeon, such as healthy and unhealthy granulations. Granulations differ greatly in size; sometimes they can only be seen with a magnifying glass, at others if exposed long to some irritation, a seton or drainage tube for example, they may become very large. They are simple or compound; the latter of larger size have secondary buds and are generally simple. At the beginning they consist simply of spherical or angular embryonic cells, uni- or multinucleated, in the midst of which are capillaries composed of embryonic cells. This initial stage lasts but a short time, soon a certain number of the embryonic cells change shape, become angular, their processes unite, and they form a network of embryonic connective-tissue cells. The meshes formed by this network are filled with an amorphous substance in the midst of which round cells are imprisoned. The cells contained in the ground substance are especially lymph cells or pus cells. In the granulations of bone there are also multinucleated mother-cells. On scraping the surface of a section of granulation tissue and

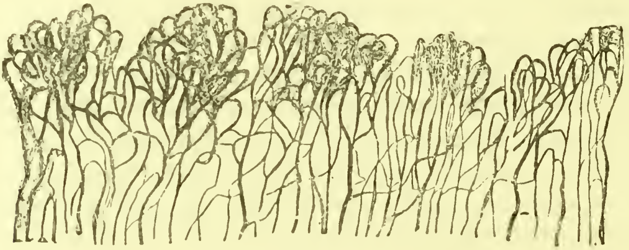

FIG. 56.—VESSELS OF GRANULATION TISSUE INJECTED.
After Billroth. Magnified 40 diameters.

examining the product in a neutral fluid spherical or angular cells are found, also cells with processes and pus corpuscles. All these are capable of amœboid movements.

The quantity of pus cells imprisoned varies according to the age of the granulations and the varying general and local pathological condition of the subject. At the beginning, pus cells are abundant; later if the granulations are red and healthy, there are fewer. When cicatrisation is slow and uncertain and the general condition of the patient bad, the granulations become grey and are said by the surgeon to be unhealthy; they then contain many pus cells. When the granulations contain many pus cells, they, to employ an old expression but one which well expresses the appearance, secrete them from their surface. How do pus cells reach the surface of granulation tissue? Are they produced on the surface, or do they travel there from the deeper parts? Hitherto there has been no direct proof of migration in the interior of granulations, but there is on the other hand proof of the migration of cells in inflamed tissues, and the secretion of pus is sometimes so abundant in a short time as to lead one to suppose that the cellular elements travel, either by means of amœboid movements, or under the influence of a current of fluid which is established from the capillaries towards the surface. This fluid transudes through the vessels, and sweeps along in its passage the free elements it meets with. The following experiment seems to us to demonstrate this fact; if after having well cleansed a wound, it be irritated by chloride of sodium or by the approach of the actual cautery, the surface is covered with a dew of little drops; in this fluid will be found pus cells which have evidently been carried

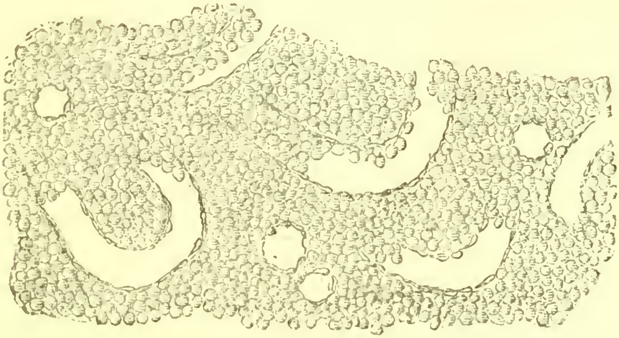

FIG. 57.—INFLAMMATORY EMBRYONIC TISSUE.
Figure borrowed from Billroth. Magnified 300 diameters.

along with it. As cicatrisation advances the pus dries up and is no longer produced in the interior of the granulations. The cementing substance of the latter condenses, fibrils of connective tissue are developed, and become organised into fibrous tissue which contracts, the granulations consequently shrinking. The adjacent granulations unite, and their blood-vessels communicating, a continuous membrane is formed.

D. **Cicatrisation of wounds.**—A wound may unite by first, second, or even third intention. In every case cicatrisation consists essentially of the formation, between the edges of the wound, of embryonic tissue which gradually passes to the state of adult tissue. After a traumatic solution of continuity, there is hæmorrhage from the divided blood-vessels. This however soon stops, and the blood coagulates in the divided vessels as far as the first collateral capillaries; it however continues to circulate in the network which remains patent. The edges of the wound undergo formative irritation which results in filling up the loss of substance with embryonic tissue. The permeable capillaries present the changes already described, namely proliferation of their cells and softening of their walls; new capillary loops spring from the old modified vessels, advance towards the wound and present a convex surface to other convex loops proceeding from the opposite side, and if the edges of the wound be kept in contact, a vascular communication is established. The cells of the embryonic tissue filling up the solution of continuity then become organised and take the form of true connective-tissue cells, the ground substance becomes fibrillar, and as resistant as that of the old tissue. Such is *union by first intention.* Although a wound of this kind may unite rapidly, there is not simple adhesion as some authors have believed; in fact, the simplest wounds, healed by first intention, leave indelible cicatrices though they may be little apparent.

In union by second intention, the granulations spring up on the surface of a wound, the edges of which cannot be kept united. These granulations, which are well formed towards the sixth or eighth day, constitute a tissue or membrane, the vessels of which anastomose from one granulation to another. When all the granulations are well united together, cicatrisation takes place by the transformation of embryonic tissue into connective tissue, as in the preceding case. The intimate mechanism is absolutely the same in both cases; in the second, cicatrisation is slower, for the granulations must have time to grow to compensate for the loss of substance. They may become grey and infiltrated with pus, or so exuberant that they have to be suppressed. The patient, in fact, undergoes all the various risks incidental to suppurating wounds.

Union by third intention differs from the preceding only by the slowness of the process, which is owing to the depth of the tissues divided, or more often to a considerable loss of substance; but the same process is at work, namely the formation of granulations. Thus there are two modes of cicatrisation of wounds; in the first, the cicatrix is formed of embryonic tissue which is organised into connective tissue as soon as the divided vessels are united, the two edges of the wound being kept in contact: in the second, a large quantity of embryonic tissue is developed and forms granulations.

Cicatricial inflammatory tissues have very various sequelæ. In the skin, a cicatrix is formed of fibrous tissue in the deep layers of which fat vesicles soon show themselves, but are never as abundant as in normal skin; the fibrous tissue is very dense. The fibrous and elastic tissue of the corium is reproduced, but the sudoriparous glands and hair follicles are never regenerated. The normal papillæ of the skin, which first hypertrophied and transformed into granulations have assisted in the formation of cicatricial tissue, return to their primitive condition as the granulations melt away and their tissue is changed from embryonic to connective tissue. This is what specially takes place in callous ulcers of the leg, the cicatrix of which, covered by a normal epidermis, shows a layer of generally hypertrophied papillæ. But if the granulations spring from deep parts and the papillæ are destroyed to a notable extent, they are not reconstituted in a complete manner and a flat or depressed cicatrix results, or on the contrary a projecting cicatrix, if the exuberant granulations have not been suppressed. Depressed cicatrices are observed after variolous pustules, syphilitic ulcers, in fact, wherever papillæ have been destroyed by suppuration. When, as often occurs in children, granulation tissues grow in an exuberant manner, projecting or cheloid cicatrices are observed.

The epidermis is reproduced on the surface of shrunken granulations at the level of the skin. Does the new epithelium spring from neighbouring epidermic cells or is it formed on the surface of the granulations? Either one or the other of these views as to the reproduction of epidermis may be supported, for though in a wound undergoing repair the new epithelium is more often developed from the periphery towards the centre, starting from the existing epithelium, islets of epithelium may also be found having no connection with the external surface. This fact may however be susceptible of another interpretation. Of late years M. Reverdin has in the case of extensive flesh wounds fixed, with slips of diachylon plaster, little flakes of epidermis lined with the rete Malpighii, on the centre of a granulating surface. In a few days a new formation of epidermis, in the form of isolated islets, is developed around the grafted epithelium. This new epithelium is developed round the graft in the same way as it is formed at the edge of a wound in continuity with normal epithelium. M. Reverdin made experiments on animals with the object of following step by step what takes place in a wound undergoing the process of epidermic grafting. He thought he observed that the transplanted epidermis acted by causing the transformation of the embryonic cells of the wound into epithelial cells. We are quite inclined to admit his explanation, recognising however that we are dealing here with a very difficult subject which may require fresh researches. We are of the opinion that, generally, epidermic cells result from the transformation of the embryonic cells of the superficial layer of the granulation tissue. Cicatricial epidermis is always very thin and is more subject than the adjacent epidermis to desquamation.

Bone granulations quickly give origin to bone tissue. The osseous cicatrix or callus will be studied when considering bone; and the cicatrisation of nerves when studying the diseases of the peripheral nervous system. We shall be content here to formulate the general law which governs the ulterior transformation of inflamed tissues. *Whenever artificial or pathological irritation causes an exuberant development of embryonic elements, and the irritation be removed, the new embryonic tissue tends to return to the primitive form of the tissue which served as a matrix.* Thus cicatrices of the skin reproduce dermal tissue, bone cicatrices bone, nerve cicatrices nerve tubes. Another still more important consideration is the seat of the new embryonic tissue at the moment that it constitutes a permanent tissue. *Whatever may be the origin of the embryonic tissue it has a tendency to reproduce the tissue of the region in which it is situated.* Thus, when a bone is extirpated in a young subject, the embryonic tissue, by which it is replaced, aids in the structure of new bone similar to that removed. As a counter fact we may cite cases where a fragment of cartilage or bone introduced under the skin disappears at the end of a few months: it is changed first into embryonic tissue, then into fibrous tissue. It might be thought *à priori* that there is here pure and simple absorption of the parts necrosed; but it is nothing of the kind. Instead of mortification, there is on the contrary an excessive formative activity of the elements which determine, first the metamorphosis of the bone into embryonic, then into fibrous tissue. Formation of a special cicatricial tissue is again under a third law: *a mass of embryonic tissue, formed in the immediate neighbourhood of a tissue of the organism, has a tendency to become organised according to the latter tissue.* This influence of propinquity is particularly well marked in osseous tissue, hyperostoses and exostoses called epiphysial are remarkable examples of it.

4.—DEGENERATIONS CONSEQUENT ON INFLAMMATION.

a. **Fatty degeneration.**—We have already seen that the disappearance of fat in the fat vesicles is a result of inflammation; on the other hand, fat granules appear in cells developed in consequence of irritation, whenever these elements are more numerous than the reconstitution of the tissue requires, or when the nutritive supply is insufficient. Thus, in the first hours of coryza, the pus cells do not contain any apparent fat; but later, when the muco-pus becomes opaque, numerous fat granules are found in the cells. In irritation of the special cellular elements of organs, for example in nephritis, hepatitis, &c., the elements, after showing some of the phenomena of hyper-nutrition or even proliferation, become infiltrated with fat granules. The proliferating elements of connective tissue may undergo analogous changes; thus, newly formed cells of the internal coat of arteries in chronic endo-arteritis are filled with fat granules, which, by the absorption of the ground substance, become free and constitute the semi-fluid contents of atheromatous foci.

b. **Gangrene.**—Gangrene consequent on inflammation is seen under two essential forms. In the first the mortified parts are eliminated entire and form so-called *eschars.* This occurs whenever there is stasis in the inflamed parts followed by coagulation of blood in the vessels, or inflammation of the arterial coats causing endo-arteritis and the formation of a clot, or when pus cells and exudation accumulating round the vessel compress it and stop the circulation. The latter condition is frequently observed in acutely inflamed osseous tissue. In subacute ostitis, necrosis is to be feared, and it occurs when an arrest of the circulation is brought about by the blocking of the Haversian canals by an exaggerated production of osseous tissue. In all such cases of gangrene, the mortified part acts on the neighbouring living tissues like a foreign body; these being irritated, embryonic tissue, pus, and granulations are produced and the necrosed part is thus isolated and eliminated. The second form is that of *progressive molecular gangrene.* It is met with in the ulceration of phagedænic ulcers, in hospital gangrene, &c.; and in the diphtheritic inflammation of German authors. It is considered to result from the infiltration of the tissues with fibrin and pus, which by compressing the blood-vessels impede the afflux of blood to the affected parts. As these lesions are localised on diseased surfaces, the superficial layer is alone deprived of life, and a molecular elimination is the consequence. Beneath the eliminated part granulations are developed, which may in turn be destroyed by an analogous process. This form of gangrene is also met with in variola. In the pustules, the papillæ may simply show a superficial formative irritation which does not prevent them being reconstituted; but when the inflammation is violent the papillæ suppurate, the infiltrated cutis is itself destroyed, and indelible cicatrix results. Generally this progressive molecular gangrene is the result of a local affection which appears to be associated with the presence of microphytes or microzoa, of which the species vary according to the nature of the disease, and are as yet insufficiently determined. Investigations on the subject are still in progress.

V.—Synthetical Study of Inflammation and its Clinical Forms.

Having analysed the various phenomena of inflammation, we may now proceed to the synthetical study of these different states and their natural grouping in inflammatory diseases.

All authors have agreed in dividing inflammation into acute and chronic. Abscess is the type of the first, cirrhosis of the liver of the second; but between these two extremes all intermediate forms may be observed, it being often difficult to define the exact limit between chronic and acute inflammation. For example, the histological phenomena of chronic catarrh of a mucous membrane approach very near to those of the same disease in the acute state, and only differ by the greater thickness and pigmentation of the membranes. A more useful and anatomical division is based on the forms of the lesions themselves, on their situation, degree of intensity and cause; and thus the following grouping may be accepted:—

I. **Congestive inflammation.**—Such are inflammatory hyperæmia, cutaneous erythema, erysipelas, acute catarrhal inflammation of the mucous membranes, rheumatic inflammation of the joints, &c. In these lesions besides congestion, proliferation and mucoid exudations containing pus cells are found; but congestion is always the predominant fact.

II. **Exudative inflammation.**—For the general study of this subject we refer the reader to what has been said regarding exudations. There should be as many different forms of inflammation as there are distinct varieties of exudation; but in reality almost all these varieties are mixed, and contain fibrin, albumen, mucus and pus cells, and may almost all be included under that form, called by the Germans, croupous exudation; such are the exudations of acute pneumonia, pleurisy, pericarditis, peritonitis, &c.

III. **Purulent inflammation.**—Purulent and puerperal infections belong to this variety. To produce this form of inflammation there must be a suppurating wound, either traumatic, or physiological like the sanious ulcers of the uterine mucous membrane at the point where the placenta is attached. In this form of infection, pus is produced in most organs with extraordinary facility and abundance, and *per contra* the congestive phenomena are but little marked. Thus, a joint may be full of pus with the synovial membrane hardly injected. The hypothesis of Cohnheim does much to explain this facile suppuration, although it is difficult to understand how such an enormous mass, often many pints of pus, can pre-exist in the blood and pass from it in the course of a few days. According to the researches of Pasteur, purulent infection is produced by a vibrio which lives in common water, and which is at the same time aerobic and anaerobic, that is to say, capable of living in air or without air. By inoculation with these microbia, pus is produced in a few hours, and a veritable abscess is formed a few days after. If the generating microbium finds a suitable medium of culture in the economy, it produces centres of suppuration in various organs and death. (Communication made to the Acad. des Sc. and to the Acad. de Med. April 1878.)

IV. **Infection, suppuration and septicæmia.**—According to M. Pasteur, septicæmia is due to another septic vibrio or microbium which he has succeeded in cultivating and reproducing by successive cultures, as he had also done with the microbium of purulent infection. This microbium is killed by oxygen; it is anaerobic. A distinction must, however, be made between the adult vibrio and the germinal corpuscles. The latter can in fact preserve their properties in spite of contact with air. The bacteria which are constantly met with in the blood of animals affected with malignant pustule (Toussaint, Davaine, &c.) are aerobic according to Pasteur, and cannot exist without oxygen. According to Pasteur, Coze and Feltz, Hallier, Cohn, Klebs, Tiegel, Tigri, &c., there are microbia possessing special characters and properties in the majority of contagious and infectious diseases. But these researches have given rise to so many denials and contradictory discussions that their conclusions cannot yet be regarded as proved.

V. **Hyperplastic or interstitial inflammation.**—This springs suddenly into existence either in the acute or chronic state by a development of embryonic tissue which gradually passes to the state of adult connective or bone tissue. Such are cirrhosis of the liver and kidney, interstitial pneumonia, sclerosis, periostoses, exostoses, &c.

VI. **Gangrenous inflammation.**—See above, page 117.

VII. **Caseous inflammation** (Förster).—In this the products of inflammation are not eliminated. They become atrophied, broken up and filled with fine fatty granules, destruction of the part affected being the result. The lungs and the lymphatic glands are the usual seat of this form of inflammation, but it may occur in all the other organs. The essential condition of its production is that the infiltrated pus should remain long in such abundance in an organ, that the vessels are compressed by the inflammatory elements. The same result occurs when inflamed vessels are themselves the seat of endo-arteritis.

VIII. **Pseudo-membranous inflammation.**—Such are the lesions of croupous laryngitis or true croup. They have been studied above (page 104).

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CHAPTER IV

TUMOURS.

TUMOURS differ from inflammatory new formations by their tendency to persist and grow, while new inflammatory formations tend always to disappear or to reproduce the tissue which served them as a matrix.

DEFINITION OF TUMOUR.

The word *tumour* (tumor, ὄγκος) has been applied in medicine from all antiquity to the most various productions. At first every swelling, every tumefaction of whatever kind, was called a tumour. Thus displacements of an organ, hernias for example, were placed among tumours, and so they are still called clinically in the pathology of the crural and inguinal regions, &c. The word was afterwards limited to abnormal tumefactions, demonstrable after death; but lesions becoming better known by means of microscopic analysis, the group of tumours became more circumscribed, as histological structure became the basis of definition.

We call a tumour *any mass composed of a tissue of new formation (neoplasm) which has the tendency to persist or to increase in size.* This definition comprehends two terms which we will analyse; the neoplasm[1] and its persistence or growth.

In a general way, neoplasms are subject to two laws: the first, which results from the labours of J. Müller may be thus stated: *The tissue of which a tumour is formed has its type in the tissue of the organism in the embryonic state or in that of complete development.* The second is from Virchow: *The cellular elements of a tumour are derived from pre-existing elements of the organism;* to which Virchow adds that *they are derived from the cells of connective tissue.*

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[1] By neoplasm is understood a tissue of new formation, whatever be its nature or origin.

Histologists of every school are now inclined to admit J. Müller's law, a law which was misunderstood at first, and still badly interpreted, even by his most immediate pupils. The first proposition of Virchow's law is true. Hazardous and hypothetical at the time that it was put forth, the assertion, that the elements of every tumour are derived from pre-existing cells of the organism, seems to us to be now perfectly demonstrated. But the second proposition of Virchow, that connective-tissue cells are the starting-point of every tumour, is not true, for they may be developed from epithelial cells and other cellular elements.

The word neoplasm, which we make use of to define tumours, distinguishes them from effusions, retention of secretions, &c., wrongly considered, we think, by Virchow as tumours. Thus a collection of blood should no more be considered a tumour than a hernia. The retention of the secretion of a serous bursa, as in hygroma, is also, in our opinion, not a tumour. For a long time infarcts were included among tumours, and Virchow does not hesitate to include among them the necrobiotic changes of the tissues consequent on obliteration of blood-vessels.

The second term of our definition, persistence and growth, distinguishes tumours from inflammatory neoplasms. In the latter case the new growths become organised by reproducing the tissue from which they are generated, or they disappear little by little by suppuration or caseation, &c. This is too important a fact to be passed over. Tumours obey, in a general way, the laws which regulate living tissues, but they live to a certain degree an independent life, and possess a special circulation. They increase and grow at the expense of the individual in whom they are implanted, so as to constitute a new organism grafted on a more complete organism. For example, a patient affected with lipoma emaciates without seeing the tumour diminish. In the same way patients affected with carcinoma emaciate and fall into a condition of incurable cachexia, whilst the tumour grows rapidly. This development and autonomy of tumours suggest the idea of parasitism. Laennec looked upon them as parasitic masses having their own individuality and developing as distinct beings.[1] This idea of Laennec is now completely abandoned, as we have already indicated by the statement of Müller's law, and if the word parasitic tumour is employed clinically, it is to specify a particular case in which parasites form a distinct mass.

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[1] The words heteromorphia, heteroplasia contrasted with homœomorphia, homœoplasia, &c., representing the idea of parasitism or tissues without analogues in the economy, seem to us useless after what we have said above regarding J. Müller's law.

CLASSIFICATION OF TUMOURS.

Müller's law, that the tissue of every tumour is the analogue of a physiological tissue in the embryonic or adult state, leads us to a classification of tumours, in which to each kind of tumour a name is given, the Greek root of which is borrowed from the analogous normal tissue, the termination *oma*, *omata*, being added.[1] But it must not be thought that J. Müller or his immediate successors or pupils have always made use of this law in the classification of tumours; often the contrary. Thus, in speaking of certain tumours, J. Müller employs the words cholesteatoma and steatoma, the radicles of which are the words cholesterin and stearin; but we may remark that sometimes the tumour called cholesteatoma does not contain either one or the other of these substances. The pupils of J. Müller have also devised and employed words which in no way recall the names of tissues, as we shall see in proceeding with our description.

Virchow, the author of the most recent and extensive treatise on this subject, divides tumours into four groups, which are :—

1. Tumours formed from the elements of the blood; for example, hæmatoma or blood tumour.

2. Tumours formed by the retention of secretions, as glandular cysts, hygroma.

3. Tumours resulting from the proliferation of the cellular elements of pre-existing tissues of the organism. This class is divided into *histioid tumours*, composed of a single tissue; *organoid tumours*, reproducing the configuration of an organ; *teratoid tumours*, resembling by the union of different organs an incomplete being. Each of these three large groups is divided and subdivided.

4. *Mixed tumours* resulting from the union of many of the preceding. The third group of Virchow's classification includes almost all tumours. We cannot admit his first group, nor the majority of those contained in the second, as being tumours at all. In a remarkable work, called the *Pathology of Tumours*, he has included almost all general pathology. We, on the contrary, wish to treat simply from the histological point of view, and

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[1] Certain well-defined tumours being designated from long use by certain names, we adopt them, not being willing to introduce new words.

have therefore included under the head of inflammation and hæmorrhage what seemed to us to rightly belong to them, blood tumours, hygromata, for example. We also think we have a right to reproach Virchow with having invented new words, drawn from gross physical characters, whereby to designate certain tumours, instead of employing words representative of the tissues. Thus he uses the word *psammoma* to signify a tumour of the meninges, because it contains calcareous granules similar to fine sand, and the word *glioma* is applied to tumours of the brain because they are of a consistency analogous to glue. He thus departs from the classification which Müller's law suggests, and which we intend to follow absolutely.

The classification made by Förster comprises :—

1. Tumours formed of a simple tissue, and sometimes even of a single element of this tissue, for example, fibroma, osteoma, &c.
2. Tumours having a complex arrangement, the analogue of which can be formed in the economy; for example, papilloma, cysts.
3. Tumours formed of cells having their analogues in the economy, but arranged in a manner other than physiological. This group includes sarcoma, carcinoma, epithelioma, lymphatic tumours, under which may be classed the organic lesions of typhoid fever, tubercle, syphilitic gummata, and true lymphoma.

Förster's classification, more particularly the third group, does not seem to us to be good, in that it does not take sufficient account of the embryonic state of the tissues, nor of their ulterior metamorphoses. Moreover, in the last group he depends on a different basis to that on which he founds the first two classes, and neglects the consideration of the tissue, taking note only of characters drawn from cells.

Our classification is based solely on the analogy of tumours with normal tissues. Thus, we recognise those analogous to embryonic, fibrous, cartilaginous, osseous tissue, &c.; and employ, as far as possible, words formed by the radicle of the normal tissues to which the terminations *oma*, *omata*, are added.

Group I.—Comprises tumours formed of a tissue analogous to embryonic tissue. We might employ a new word to indicate this analogy, but we prefer to make use of the old word *sarcoma*, though it has been employed in very different senses by different authors. This group only contains one genus, sarcoma, of which there are a great number of species and varieties.

Group II.—Contains tumours formed of a tissue, the type of which is found in connective tissue. This tissue is sometimes mucous, and the tumour is called *myxoma*, sometimes fibrous and called *fibroma* (Verneuil), or *inoma*, from ἰνὸς, fibre (Paget), sometimes adipose, when called *lipoma*. In some cases the tissue undergoes hypertrophic aberration affecting the size of the cells; this is the case in *carcinoma*, which would be better called *alveolar fibroma*; in others, the cells atrophy, as in *tubercle*, *glanders*, and *syphilitic gummata*. This second group therefore contains the varieties *myxoma*, *fibroma*, *lipoma*, *carcinoma*, *tubercle*, *glanders* and *syphilitic gummata*.

GROUP III.—Contains tumours formed of cartilaginous tissue, of which there is but one genus, *chondroma*.

GROUP IV.—Is composed of tumours formed of osseous tissue, *osteoma*.

GROUP V.—Tumours, formed of muscular tissue or *myoma*, are divided into two kinds, according as the fibres of new formations are striated or non-striated: *myoma of striated fibres*, *myoma of non-striated fibres*.

GROUP VI.—Tumours formed of nervous tissue are of two varieties: the *medullary neuroma* containing nerve cells, and the *fasiculated neuroma* containing nerve tubes.

GROUP VII.—In this are tumours formed of blood-vessels or *angioma*.

GROUP VIII.—Contains tumours formed of lymphatic vessels, *lymphangioma*, and those which reproduce the structure of lymphatic glands, *lymphadenoma*.

GROUP IX.—Contains tumours composed of epithelium of new formation. They are divided into four varieties according as the cells are arranged in irregular masses, *epithelioma*, or in papillæ, *papilloma*, or in culs-de-sac, *adenoma*, or in cavities of new formation, *cysts*.

GROUP X.—Contains *mixed tumours*, containing a great number of tissues; they are formed specially during intra-uterine life.

The classification of tumours which we propose differs, it will be seen, notably from those hitherto published. It is an anatomical classification. It cannot consequently serve to determine the degree of gravity of a tumour. No anatomical classification can at present answer this legitimate desire of the physician. To determine the degree of gravity of a tumour, knowledge of the order, species, and variety to which it belongs can alone be depended upon. The sole general consideration, which may be advanced on the subject of the benignity or malignity of tumours, is that the most serious are those which determine the formation of a large quantity of embryonic elements, at the expense of which they grow rapidly. Our classification has the advantage of being purely histological and of being based on one law and on one consideration which seems to us to be supreme, that is, the general arrangement of the morbid tissue and the distribution of the elements composing it.

I.—TUMOURS FORMED OF EMBRYONIC TISSUE.

Sarcoma.

We will first study the generic character of tumours analagous in structure to embryonic tissue, and then discuss the characters belonging specially to each species and variety.

Synonyms.—There are no tumours which have received a greater number of names than the sarcomata. J Müller partly described them under the name of *fibro-albuminoid tumours.* Lebert, having remarked that many of these tumours contained an abundance of fusiform cells, called them *fibro-plastic tumours.* Charles Robin thought that fibro-plastic tumours should be separated from certain tumours having numerous analogies with them but differing from them in the round form of their cells, and he called them *embryo-plastic tumours.* Paget gave to fibroplastic tumours the name of *recurring fibroid*, and grouped them with certain tumours having a structure analogous to that of the medulla of bone, which he called *myeloid tumours.* These latter were called by Charles Robin *tumours of medulla-cells*, and *tumours of myeloplates.* Finally, Virchow separated from sarcoma certain tumours which had always been classified with them and gave them the names of *glioma* and *psammoma.*

Definition.—We define sarcoma as *a tumour formed of embryonic tissue either pure or undergoing one of the first modifications it shows previous to becoming adult tissue.* Thus, when embryonic tissue is changed into fibrous tissue, from the spherical form its cells become elongated and fusiform, and an amorphous ground substance is thrown out between them. This is an embryonic state of connective tissue, and tumours showing an analogous structure are called sarcomata. Though sarcomatous tissue has its type in the physiological condition, its analogue can also be found in the pathological condition during inflammation. Thus, in granulation tissue all the embryonic phases of connective tissue are met with; certain sarcomata have a similar structure. Further, if inflammatory tissue arises in the medulla of bone, it shows when granulating, cells identical with those of the medulla of bone and often osseous trabeculæ in the process of development; identical forms are met with in certain sarcomatous tumours. The difference between sarcoma and inflamed tissue consists essentially in the origin and termination of the two morbid processes. When inflamed tissue originates in a wound, or chronic disease of the bones or joints, the end will be elimination or reconstitution of the permanent normal tissue, in one word recovery; while sarcoma will continue to grow indefinitely. As to the histological elements of these two neoplasms, they are, we repeat, generally identical, but often larger in sarcoma than in the inflammatory neoplasm. If, however, the latter develops slowly, the cellular elements may be as large. Further, the form of the cells in sarcoma is not entirely subordinate to the seat of the tumour; thus, in sarcoma developed in the skin or a gland large mother-cells, similar to those found in inflamed medulla of bone, may be observed. Almost the whole mass of a sarcoma is composed of cellular elements, hence Förster classifies these tumours among those solely composed of cells.

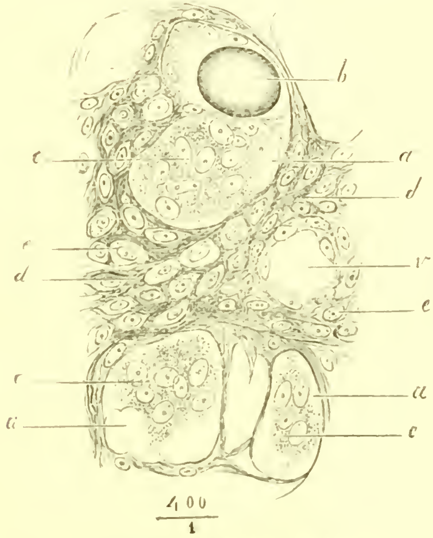

Fig. 58.—Inflamed Tissue.

a, *c*, embryonic cells occupying the place of adipose cells, one of which shows at *b*—a drop of fat; *d*, *e*, embryonic tissue; *v*, vessel, the wall of which is formed of cells which are themeslves embryonic.

General description of the genus sarcoma.—Sarcoma cells assume the most varied forms. Sometimes they are spherical, especially if examined in water—the same element which is angular in a neutral fluid may swell and become round in water; at other times the cells are irregular, containing one or many ovoid nuclei, and furnished with processes which often anastomose (figs. 59 and 62); many of the cells are fusiform with ovoid nuclei (*a*, fig. 60); in certain cranial tumours they are flat, extremely thin, variable in size, and have one central lenticular nucleus; seen full face they appear plaited and folded over like a handkerchief taken up by one corner; observed sideways they look like a fibre with a central elongated nucleus (*vide* fig. 73, p. 146). It is thus seen that the form of the cells of the genus sarcoma is very complicated; in size they may vary from 5 μ to 50 μ, or even more. The structure of the cells is simple. They have one or many nuclei which are spherical or oval and of a size varying between 5 μ and 9 μ; the nucleoli are generally small and brilliant, but they may exceptionally be as large as 5 μ. The number of nuclei in one cell varies from one to fifty; they are

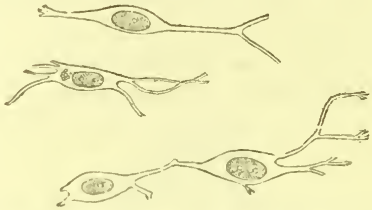

FIG. 59.—SARCOMA CELLS WITH RAMIFYING AND ANASTOMOSING PROCESSES.

Magnified 25 diameters.

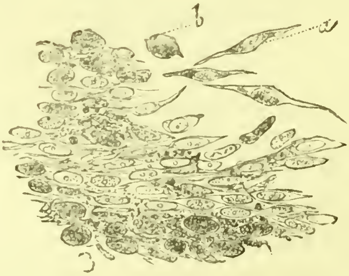

FIG. 60.—CELLS AND TISSUE OF MELANOTIC SARCOMA.

a, fusiform cells; *b*, round and deeply tinted cell.

found in these large numbers in cells, flat or otherwise, called *giant cells*, described by J. Müller in sarcoma by the name of *mother-cells*, and called *myeloplates* by Robin, in consequence of an erroneous interpretation which led him to look upon them as plates and not as cells; around the nucleus is a granular substance;

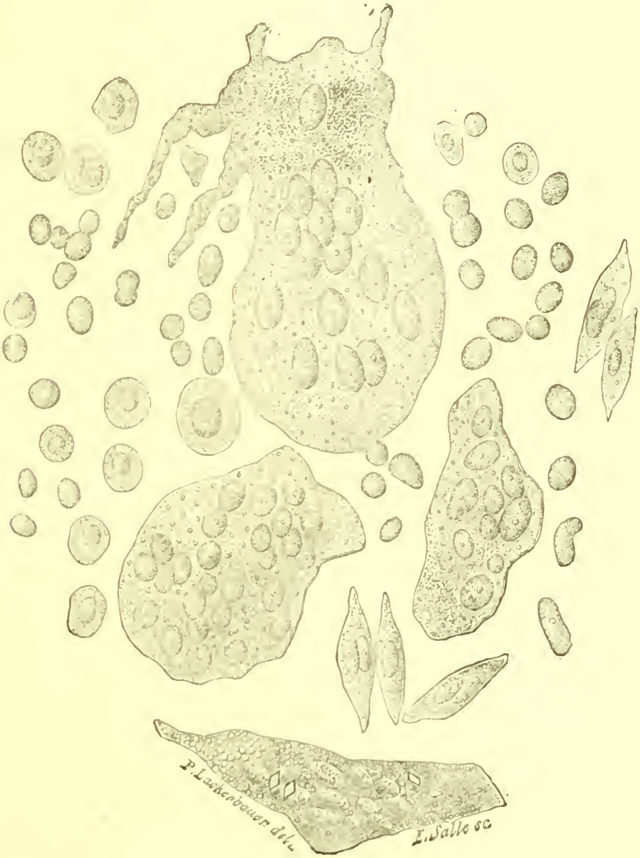

Fig. 61.—Mother-cells, Round and Fusiform Cells, from a Myleo-sarcoma of Bone.

Figure borrowed from Ordonez.

examined in a neutral fluid the nuclei are often indistinct, but on the addition of water or acetic acid they become clearly visible. The cells have no membrane and on the addition of acetic acid they swell and become extremely transparent and very indistinct. In some cases the albuminoid granules of the cell are arranged in such a way that a kind of striation is produced coarsely resembling that of a muscular fibre, but it disappears on the addition of acetic acid. Sarcoma cells like embryonic cells are very sensitive to the action of reagents; their friability is such that on scraping, the cells are ruptured and the nuclei set at liberty. Observations made in this way have led certain micrographers to admit the existence of free nuclei, which were in fact artificial products or the result of cell destruction. If a small portion of a tumour be put in a few cubic centimetres of a 33 per cent. solution of alcohol, and dissociated twenty-four hours afterwards, free nuclei are not found, but the cells are isolated and show exactly the same forms they have in the tumour itself. They can then be stained with picrocarminate of ammonia and preserved for an indefinite period, provided that the glycerine has been allowed to penetrate slowly. Sarcoma cells are thus seen to be of such various forms and sizes that they are little characteristic when examined alone, so that the anatomical diagnosis of sarcoma cannot be made from elements obtained by scraping.

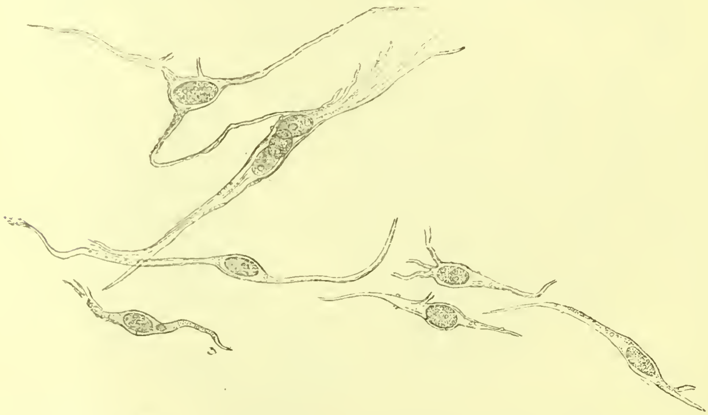

FIG. 62.—SARCOMA CELLS ISOLATED IN A 33 PER CENT. SOLUTION OF ALCOHOL AND STAINED WITH PICRO-CARMINATE OF AMMONIA.

They show very long and multiple processes. One of them has three nuclei. Magnified 300 diameters.

Sarcoma is defined and characterised by the arrangement of the elements and their mutual relations to one another. The cells are placed one beside the other, either touching or separated by an amorphous substance, which is soft and small in quantity. Of all tumours, sarcoma is the only one with so simple a structure, a veritable embryonic organisation. The blood-vessels are numerous, and are in direct relation with the cells; some of them however, and particularly the large vessels, are surrounded by fasciculated connective tissue; they have no regular arrangement, and their structure is similar to that of blood-vessels in inflamed tissues, their cells being embryonic. In soft sarcoma, in spite of the softness of the tissue, it is impossible to isolate the vessels. This is owing to the fact that the cells of their walls are embryonic and not distinct from those composing the mass of the tumour; if an attempt be made to separate them by dissociation, they have no resistance and their elements are dissociated together with those of the tumour. Blood-vessels may be isolated in a fresh state from a sarcomatous tumour which is tending towards a higher stage of organisation. After hardening[1] such a tumour, and

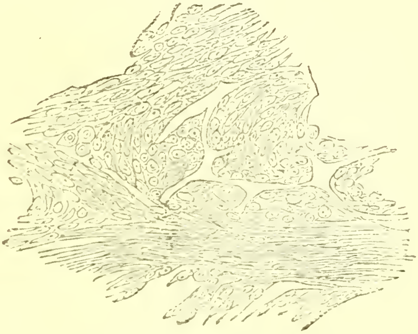

FIG. 63.—SECTION OF A FASCICULATED SARCOMA.
Magnified 200 diameters. Figure borrowed from Rindfleisch.

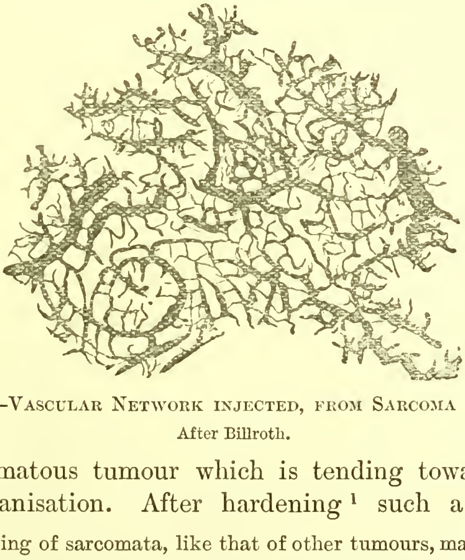

FIG. 64.—VASCULAR NETWORK INJECTED, FROM SARCOMA OF BONE.
After Billroth.

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[1] The hardening of sarcomata, like that of other tumours, may be obtained by different methods. The simplest consists in placing portions of the tumour in strong alcohol at 90°; twenty-four hours afterwards they are sufficiently hard to allow of sections being made, which may be stained with ammoniated carmine, or with a 1 per cent. solution of picrocarmine. With the latter reagent staining is

examining fine sections with a power magnifying 150 or 200 diameters, the lumen of the divided vessels is seen to be bounded by round or fusiform cells, but the walls properly belonging to these canals can rarely be made out. This is an essential point, and, together with the general arrangement of the elements, is characteristic of sarcoma, and explains the facility with which vascular ruptures and effusions occur, as well as the formation of blood cysts so frequently observed in these tumours.

Species and varieties of sarcoma.—The form of the cells, the cementing substance, the blood-vessels and the scheme of organisation of the morbid tissue, form the bases for the classification of the species and varieties of sarcoma. A sarcoma is not always composed of a single kind of cell; every form described above may be met with, and there is perhaps hardly a sarcomatous tumour in which some of those cells, known in France under the name of *myeloplates*, may not be ultimately discovered. If, therefore, in classifying tumours use is to be made of the form of the cellular elements present, the presence of such or such cells should not alone be considered, but the proportion in which they are found. The intercellular substance is sometimes semi-fluid, so that the molecules may be displaced, and in this case pressure being equal in every direction, the cells are round. At other times there is no ground substance or it is more or less solid, and the cells may then be pressed one against the other and take various forms. If they are compressed laterally in both directions they elongate and become fusiform with two plane surfaces; if compressed

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almost instantaneous, it being sufficient to put a drop of the solution on a thin section placed on a slide, to cover it, and add glycerine. With a little dexterity very beautiful preparations are obtained by this method, but preparations simply hardened in alcohol are never hard enough to resist much pressure, so that if it is necessary to use a microtome recourse must be had to the following method: let the pieces remain twenty-four hours in alcohol, after which put them in a saturated solution of picric acid, and then into a weak solution of gum arabic, where they should remain twenty-four hours; then let them be put again into alcohol for another twenty-four hours; the alcohol, coagulating the gum which has penetrated into the interstices of the tissues, completes the hardening process. Perfect hardening may also be obtained by leaving the tumour in a ·2 per cent. solution of chromic acid for one or two weeks. A solution of bichromate of potash or ammonia also hardens tumours, whilst preserving the form of the elements; only they must be immersed for many months, at the end of which time, if the hardening be not sufficient, recourse must be had to the successive action of gum and alcohol. The elements of sarcomata and other tumours, subjected to the process of hardening by chromic acid or the bichromates, stain badly with carmine, but staining of the cells and nuclei can be obtained by means of hæmatoxylin and purpurin. It should be added that before attempting to stain the sections made after hardening in gum, they must be soaked for some time in water.

only in one direction, they are flattened. These facts, noted in the first edition, have since been confirmed and verified by Neumann. We must also consider as an important element in the classification of sarcoma the scheme of organisation of the embryonic tissue composing it. This scheme of organisation may be after the type of fasciculated connective tissue, neuroglia, medulla of bone, or osseous tissue. Account must also be taken of changes in the vascular walls; the blood-vessels are sometimes embryonic, dilated in a pouch-like or fusiform manner (erectile sarcoma), or sometimes ruptured producing blood cysts; at other times, on the contrary, the walls are resistant and even infiltrated with calcareous salts (angiolithic sarcoma). These elements in the classification of the species of sarcoma being recognised, the following is what we propose:—

1st Species. Encephaloid sarcoma.—When sarcoma is solely formed of embryonic tissue, its ground substance soft and small in quantity, and its cellular elements globular and small, it is said to be encephaloid, for the tumour resembles softened cerebral substance (the *embryoplastic tumour* of Robin).

2nd Species. Fasciculated sarcoma.—If the ground substance is thicker and more solid, and the elements fusiform presenting the first stage of the transformation of embryonic into connective-tissue cells (connective-tissue fibres may even be formed), it is fasciculated sarcoma (the *tumour of fibro-plastic cells* of Lebert).

3rd Species. Myeloid sarcoma.—Especially in bone but also sometimes in other organs, the morbid mass is composed of a tissue similar to embryonic bone marrow; this is myeloid sarcoma.

4th Species. Ossifying sarcoma.—In a certain number of sarcomata the embryonic tissue shows a tendency to become organised into a more or less perfect bony tissue; such are ossifying sarcomata.

5th Species. Neurogliac sarcoma.—In sarcoma of the nervous centres, and occasionally in other organs, the embryonic tissue has a tendency to take the form of neuroglia; this is neurogliac sarcoma (*glioma* of Virchow).

6th Species. Angiolithic sarcoma.—In the meninges, sarcoma tends to take the vascular arrangement of the choroid plexus, and shows the peculiar buddings and calcareous granules which are physiological in the choroid plexus; we call this form angiolithic sarcoma (*psammoma* of Virchow).

Such are the species based on histological forms properly so called; but the three following species of sarcoma may also be considered as distinct, though they present but purely nutritive modifications of their elements. They are :—

7th Species. Myxo-sarcoma, in which the cells have undergone mucoid degeneration.

8th Species. Lipomatous sarcoma.—This is a sarcoma in which the cells are filled with droplets of fat which distend without destroying them, as in the subcutaneous cellulo-adipose tissue; such is the *lipo-sarcoma* of Virchow or lipomatous sarcoma.

9th Species. Melanotic sarcoma.—The cells have undergone a very important change, which consists in their impregnation with pigment granules.

What justifies the distinction of the various species given above is the fact that all possess the property of producing secondary growths *in situ* or far from their point of origin, having the same characters.

Independently of these principal species, in each, varieties may be distinguished, based on nutritive changes in the cells. These disorders of nutrition are as follows :—

a. **Fatty degeneration.**—This is general at the centre of most large and old tumours; the cells are then infiltrated with fine proteid and fatty granules which bring about their destruction. The sarcomata which show this change must not be confounded with those described under the name of lipomatous sarcomata.

b. **Infarction.**—In certain large sarcomata, white opaque caseous masses are observed, often of very irregular form; the blood-vessels are also seen to be filled with a fatty granular pigmented detritus, while at the same time the cells are compressed and contain fat granules. This state, which is consecutive to obliteration of the blood-vessels of the altered part, may be considered as a kind of infarct.

c. **Calcareous degeneration.**—In sarcoma developed at the expense of osseous tissue and periosteum, or sometimes far from bony tissue, a more or less considerable calcareous transformation of parts of the tumour may be observed. This metamorphosis is often shown in the form of calcareous radiating needles, or irregularly arranged stalactites. This impregnation with calcareous salts begins, as in every similar case, in the ground substance; the cells, preserved at first in the midst of little solid frameworks, ultimately also become implicated. These are retrograde phenomena ending in the cessation of nutritive functions in part of the tumour; they must not be confounded with ossification, that is to say the formation of true osseous tissue, which takes place in ossifying sarcoma.

d. **Formation of blood cysts.**—The transformation of a part of the tumour into blood cysts is brought about when the blood-vessels, having no proper resisting wall, are ruptured and extravasation of blood follows ; a hæmorrhagic focus is thus produced, and the cells that have undergone mucoid degeneration mix with the elements of the blood. This complication is very frequent in the soft varieties of sarcoma.

e. **Inflammation.**—When a sarcoma is irritated, all the phenomena of inflammation are observed. In virtue of its embryonic structure it is more than any other tissue disposed to inflammation and suppuration. Sarcoma has a great tendency to exuberant growth and to give rise to voluminous granulations ; this is the villous variety of sarcoma. Every sarcomatous tumour situated on a surface tends to become villous.

It is a curious fact that osseous tissue, already existing in a schematic manner it is true in sarcoma, may under the influence of irritation disappear by absorption of its ground substance, and return to the embryonic state. Another equally interesting fact is that when a sarcoma has rendered a bone friable and fracture occurs, a new production of cartilaginous tissue is often seen to take place at the expense of the tumour, just as if an ordinary fracture had occurred. We will now study in detail each one of the species sketched above.

Encephaloid sarcoma.—This was formerly confounded with carcinoma under the name of encephaloid cancer. It is often called in France by the name of embryo-plastic tumour. The encephaloid appearance of these tumours and their pulpy consistence are often well marked ; they are of a grey or greyish-white colour and often more or less translucent. The primary tumour very quickly acquires an enormous size, and may become generalised and give origin to secondary masses, particularly in the lung. The blood-vessels are large and the walls embryonic ; they are often dilated, varicose or aneurismal, when they appear to the naked eye as little red points ; they may finally be ruptured and give rise to small cysts filled with fluid or coagulated blood mixed with mucus, and holding retrograde elements in suspension ; the vascular walls often give way and ecchymoses or diffuse hæmorrhages are produced. In most of these hæmorrhagic foci the red blood corpuscles are preserved, and there is no pigmentation of the neighbouring elements ; it seems as if circulation still takes place in these irregular lacunæ. If the surface of a section be scraped directly after separation of the tumour from the living subject, the fluid obtained is quite transparent—but twenty-four or forty-eight hours after removal scraping yields an abundant white fluid similar to cancer juice; this milkiness is due to the fact that the embryonic cells of the tumour have been set free, in consequence of a cadaveric liquefaction of the ground substance. It is thus seen that this character, formerly given as peculiar to cancer, may be met with in certain sarcomata, examined some hours after death.

The cells of encephaloid sarcoma are generally small, round or more or less irregular, and may have a diameter of 30 μ; their nuclei, which sometimes measure more than 10 μ, contain one or more nuclei; they never have the same variety of form as carcinoma cells; they consist of a mass of protoplasm surrounding one or more nuclei, a vesicular condition of which, or of the cellular substance, may sometimes be observed. In encephaloid sarcoma there is often found a certain amount of old connective tissue which was pre-existent at the spot where the tumour was developed. Besides the nutritive changes indicated above, in the earliest-formed parts of these tumours the cells are often found infiltrated with fine fat granules, and larger granules of the same kind are found united in the form of granular bodies. Parts of the tumour may undergo mucoid or calcareous degeneration, or become infiltrated with red or black pigment. In tumours where these changes are very limited, and which cannot consequently be classified among primary mucous or melanotic tumours, to the name encephaloid sarcoma, signifying the species, should be added a term describing the partial degeneration observed; thus, for example, *encephaloid sarcoma with partial mucoid degeneration.*

The seat of encephaloid sarcoma is very variable; it may be observed in the skin, the subcutaneous cellular tissue, the bones, muscles, glands, and especially in the breast and testicle. The most serious form of sarcoma is that which relapses most frequently, and is generalised in a great number of organs.

Fasciculated or spindle-celled sarcoma.—In this species the embryonic tissue has already undergone an attempt at organisation and evolution in the direction of connective tissue: this is the *fibro-plastic tumour* of Lebert. As this species is very common, it is usually regarded as the type of sarcoma. Some surgeons have made embryo-plastic tumours a sub-variety of fibro-plastic tumours, which is a senseless classification when looked at either from Lebert's or our own point of view. From the translucence of these tumours and their fasciculated appearance they have been compared with flesh, and hence the name sarcoma, a name afterwards applied to the whole genus; the word is bad from an etymological point of view, though defended by use.

The cells of fasciculated sarcoma are fusiform, terminating in two long, sometimes ramifying, extremities. Their dimensions are variable; they have a mean length of 15 μ to 30 μ, but they may attain the enormous size of 100 μ. Perhaps it would be convenient, as Rindfleisch has done, to classify these tumours according as they have small or large fusiform cells.

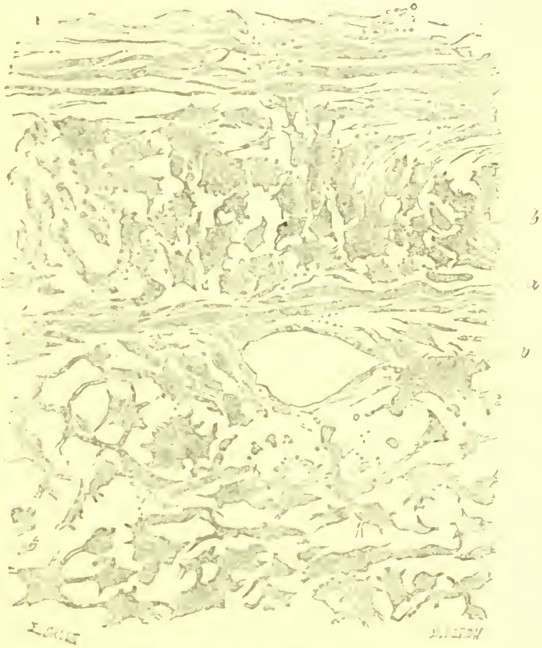

FIG. 65.—SECTION OF A FASCICULATED SARCOMA.

a, sarcoma cells arranged in bundles and seen sideways; *b*, cells belonging to bundles lying perpendicular to the first and seen full face; *v* blood-vessel showing in its wall a series of flattened cells. Magnified 200 diameters.

The tissue of fasciculated sarcoma is very simple. The cellular elements are so arranged that they are in contact, the extremities of one cell being in relation with the dilated portion of neighbouring cells. Cells unite so as to form veritable fasciculi, which are sometimes parallel to one another and sometimes crossed. The genreal direction of the blood-vessels is the same as that of the cells. When seen in section, vortices or pellets are observed, separated and surrounded by longitudinal tracts. The vortices represent the transverse section of fasciculi, the interposed tracts their longitudinal section (*vide* fig. 65). The centre of the vortices often makes a conical projection after section, an appearance which we shall see more marked in fibrous tumours.

The periphery of these tumours is sometimes well defined as in fibroma, sometimes diffused, the morbid mass being continuous without interruption with the neighbouring normal tissues. They grow from the periphery, sometimes irregularly, sometimes by distinct spherical lobules. Their size varies, but they are generally smaller than encephaloid sarcoma; in the limbs, however, fasciculated sarcoma, springing from the periosteum, is often found to reach the size of the head of an adult. In the fresh state they have no juice, but a day or two after operation, or in the cadaver, a little juice is observed, less abundant than in encephaloid sarcoma, and also less abundant and less thick than in carcinoma, where it may be squeezed out by pressure like a milky exudation.

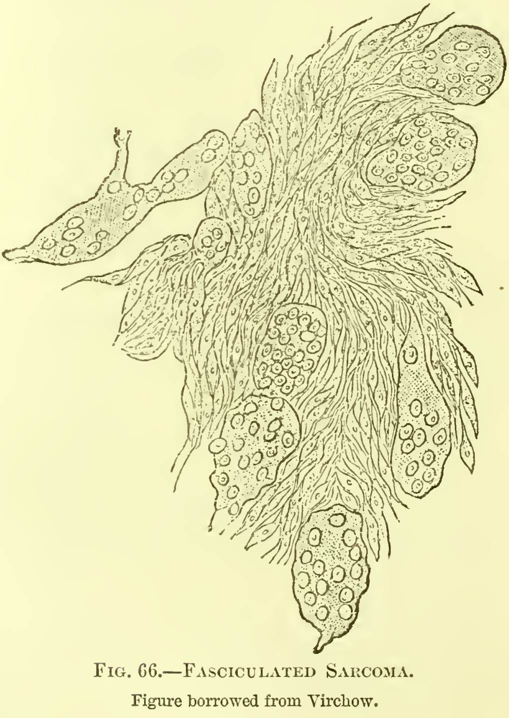

Fig. 66.—Fasciculated Sarcoma.

Figure borrowed from Virchow.

Fasciculated sarcoma is often seated under the periosteum; it is also found in bone, connective tissue, muscles, the breast, testicle, &c., and may become subsequently generalised in all the organs. In the breast this, and also the preceding form of sarcoma, is accompanied with proliferation of the cells of the glandular culs-de-sac. Hence Billroth made a distinct variety—*adeno-sarcoma*. In France when situated in the breast it is often wrongly called adenoma of the breast, a confusion constantly made by Velpeau. A great number of different tumours of the breast have been confounded, under the name of adenoma, or adenoid tumour.

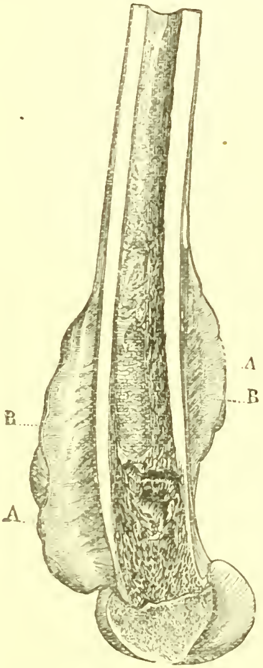

Fig. 67.—Fasciculated Sarcoma of the Periosteum.

Two forms of sarcoma of the breast are recognisable. The tumour may form a mass through which the culs-de-sac are disseminated, *massive sarcoma of the breast*, or the sarcomatous tissue buds, and pushes back the walls of the canals and the glandular culs-de-sac, bulging into their cavities. Budding protruding masses are thus formed, and the galactophorous ducts and acini being increased in size, they are transformed by these into lacunar cavities, into which the buds of the sarcoma project, *budding sarcoma of the breast.* These buds and cavities are covered by pavement or cylindrical epithelial cells. The lacunar cavities are of variable size, and appear in section like stellate or semilunar fissures, or they may appear as large spaces separating the tumour into lobes. Their walls are thin, smooth, and always lined with epithelial cells, which we have succeeded in staining with nitrate of silver. Twenty-four hours after death, on scraping the surface of a section of tumour, an abundant milky fluid is obtained; it is well to know of this character, if the juice of a tumour be considered of importance in determining its malignity. Tumours of the same character may be developed in the testicle and give rise to the same phenomena.

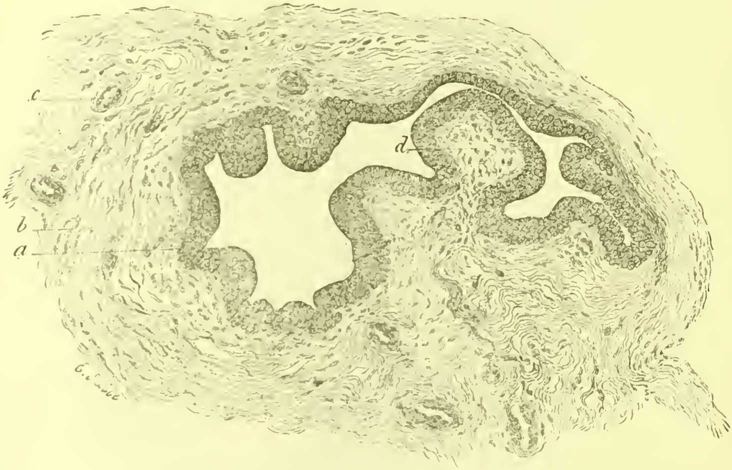

FIG. 68.—BUDDING FIBROMA OF THE BREAST.

d, bud projecting into a galactophorous canal; *a*, epithelial investment of this canal; *b*, connective tissue.

The adeno-sarcoma of Billroth ought not to be looked upon as a distinct species. In fact when sarcoma of the breast containing glandular culs-de-sac is removed surgically, and recurs, the new tumour will no longer contain glandular elements, or a very small number. If the tumour becomes generalised in other organs, the secondary growths never have glandular culs-de-sac. In sarcoma of the breast or other organs, adipose tissue is never found in the midst of the morbid mass. We shall see later that this character is important, differentiating sarcoma, by the naked eye, from carcinoma, where, on the contrary, adipose islets are often observed in the midst of the morbid tissue.

Myeloid sarcoma (*myeloid tumour* of Paget, the *tumour* *of medulla-cells and myeloplates* of Robin).—Myeloid sarcoma is a soft tumour, the cells of which are in contact, without the interposition of intercellular substance, or of a very slight amount: the cells are similar to those of the preceding species (*vide* figs. 59, 60, and 62). Some are small and spherical like cells of embryonic medulla or of every embryonic tissue, particularly encephaloid sarcoma; these are the *medulla-cells* of Robin: others are fusiform, and sometimes, large, irregular, flat cells may be seen with oval nuclei, *myeloplates* (*vide* figs. 61 and 66). It is essential to notice, however, that these latter elements are not peculiar to myeloid sarcoma; they are found, in small numbers it is true, in encephaloid and fasciculated sarcoma of various organs; in the breast and testicle, for example. Finally, some cells of myeloid sarcoma resemble elements which have been rendered angular by reciprocal pressure, called *osteoblasts* by Gegenbauer.

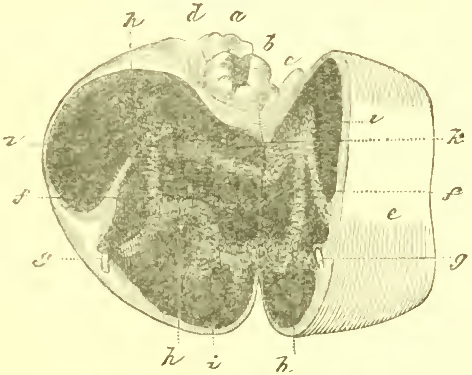

Fig. 69. Myeloid Sarcoma of the Maxilla.

Figure borrowed from the 'Surgical Pathology' of Nélaton.

The seat of myeloid sarcoma is always in the bones. It is generally limited to a single bone, which it may destroy completely, and transform into a red soft mass, its course being only arrested by the deep calcified layer of the articular cartilage. Tumours, formerly called aneurisms of the bone, are often myeloid sarcomata, the blood-vessels of which have dilated and ruptured, so that the blood circulates in a cavernous system.

Ossifying sarcoma.—This species is very similar to the preceding. It differs from it in the tendency the tumour has to ossify. The ossification is never complete; some osseous trabeculæ only are produced limiting alveoli filled with the tissue of myeloid sarcoma.

The little tumours of the alveolar processes called **epules** are sometimes myeloid, sometimes ossifying sarcomata. These tumours, covered by buccal mucous membrane, present in the midst of their mass, or at the periphery, more or less complete osseous trabeculæ, in the form of radii irregularly arranged, or diverging from their base of implantation. These trabeculæ are surrounded on all sides by an embryonic tissue similar to young medulla; in their interior true bone corpuscles are seen with well-marked anastomotic processes, more numerous and broader than those of physiological osseous tissue. At the periphery of these osseous trabeculæ, it is not unusual to see young cells situated half within the medullary tissue and half within the bone which has overtaken them in the process of development. Finally the osseous trabeculæ, in process of development, are always implanted on the old bone and spring from rigid fibres. These fibres, the arciform fibres of the ossifying shell, Sharpey's fibres when present in bone, exist in such great numbers in epulis that they form the largest part of the tumour. It may be asked if epulis is an osteoma or sarcoma. It belongs to the genus osteoma by the property which it possesses of generating bone, but bone transformation is never perfect in these tumours; there is simply an attempt at ossification. Hence we include it among sarcoma.

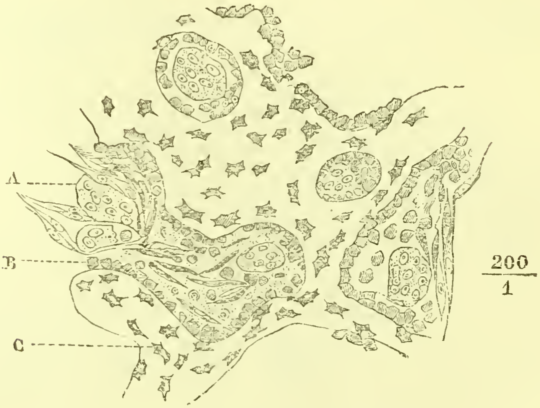

FIG. 70.—TRANSVERSE SECTION OF THE OSSIFIED PART OF AN EPULIS DECALCIFIED IN CHROMIC ACID.

A, medullary and fibro-plastic cells. B, layer of embryonic cells ranged and pressed against the new osseous trabeculæ. C, bone corpuscles.

The little tumours known as **sub-ungueal exostoses** have a structure analogous to that of epules. They, however, habitually contain cartilaginous islets, at the expense of which, or in part

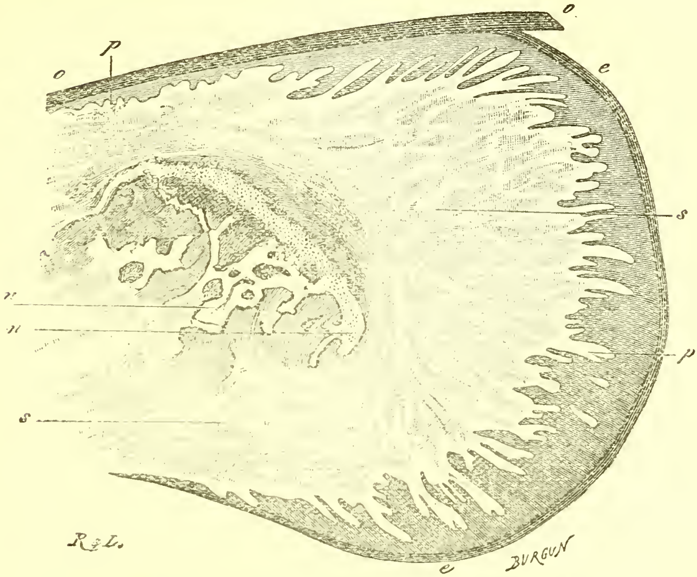

Fig. 71.—Section of a Sub-ungueal Exostosis of the Big Toe.

o, nail; *e*, epidermis and malpighian layer; *p*, hypertrophied papillæ of the cutis; *n*, *n*, osseous trabeculæ; *s*, embryonic tissue. Magnified 25 diameters.

at least, are produced the osseous trabeculæ of new formation.[1]

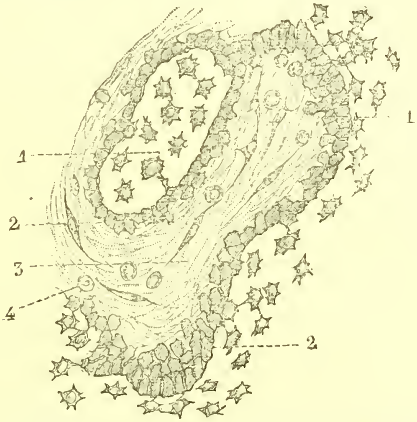

Fig. 72.—Ossifying Part of the Tumour represented at *n* in the preceding Figure.

1. Osseous trabeculæ and bone corpuscles. 2. Medulla cells arranged along the osseous trabeculæ; it is seen that many of these cells are about to become bone corpuscles. 3, 4. Connective-tissue elements.

These tumours, which sometimes relapse, never form perfect bone;

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[1] Vide *Note sur exostoses sous-unguéales* in *Jour. de l'Anat.*, Robin, 1867.

they only show a tendency to ossification. Ossifying sarcoma selects the spongy tissue of bone as its favourite seat; the big toe, the fingers, the maxilla, and the long bones, are attacked by it, especially their epiphysial extremities. The osseous trabeculæ it contains must not be confounded with growths simply encrusted with calcareous salts, though differentiation is not always possible with the naked eye. On isolating the needles incrusted with calcareous salts, found in certain encephaloid or fasciculated sarcomata, they may be seen under the microscope to be composed of a substance impregnated with calcareous granules, and hollowed into little ovoid or spherical cavities without prolongations; these little cavities, which are not bone corpuscles, for they have no anastomotic canals, serve to lodge the sarcoma cells.

Neurogliac sarcoma or glioma.—Virchow gave the name of glioma to this variety of tumour on account of its glue-like consistence, and, as he found its tissue similar to that of the neuroglia, he classified it apart from sarcoma. He, however, implicitly recognised its analogy with the latter when he created the varieties *glio-sarcoma* and *sarco-glioma.*

This tumour is composed of cells, measuring from 6 μ to 12 μ, consisting of a nucleus and a very small amount of protoplasm. Round the cells delicate filaments can be distinguished, which are connected together so as to form a reticulum. This reticulum is never seen in fresh preparations, but only after hardening with alcohol or chromic acid ; it is, in part at least, artificial, for in two preparations made by us from the same tumour, one after hardening in picric acid, and the other in chromic acid, it was only visible in the latter. We may add that in other specimens of sarcomata, which have been well hardened, an analogous reticulum may be recognised in certain parts. It is therefore not characteristic. Small free cells, recalling by their characters and reciprocal relations those of encephaloid sarcoma, are present in the meshes of the reticulum. It is, however, rare that the entire mass of one of these tumours is formed of tissue thus reticulated ; frequently isolated regions are found having the structure of encephaloid or fasciculated sarcoma. We are therefore only able to recognise in glioma a sarcoma, the tissue of which shows a tendency to organisation similar to that of neuroglia. The centre of these tumours has generally undergone fatty degeneration, so that in the brain we might at first sight hesitate between masses of tubercle and sarcoma. But fatty degeneration in the latter does not cause atrophy and dryness similar to what it does in tubercle ; in sarcoma, fat granules are accumulated in large granular bodies, and the blood-vessels are not generally obliterated, while this is always the case in tubercle. The blood-vessels of neurogliac sarcoma often have lymphatic sheaths, which are easily seen, for the vessels are isolated with facility from the surrounding tissue.

Neurogliac sarcoma is found in the brain and spinal cord, both in the white and grey matter; it may also be developed along the course of the cranial nerves and in the retina; and it often projects into the cavities of the cerebral and spinal ependyma. Virchow reports a case of glioma, observed by him, in the cortical substance of the kidney. Like all other sarcomata, the neurogliac variety often shows mucoid degeneration causing the formation of pseudo-cysts.

Angiolithic sarcoma.—This very curious species, which differs by the form of its cells from all those hitherto studied, is only observed in the cranium, vertebral canal, the parietal and visceral arachnoid, and in the pia-mater and dura-mater. The tumours contain cerebral sand similar to that met with in the choroid plexus. In the physiological condition, the blood-vessels of the choroid plexus have on their walls buddings or ampullar dilatations lined by the pavement epithelium of the ependyma; they are formed of flat cells encrusted, in the adult, with calcareous salts, so as to form true phleboliths. It is the presence of analogous buds or concretions in the blood-vessels of sarcomata which justifies the name of angiolithic, which we propose to give them. During development these tumours are soft, and easily crushed, although they contain no juice. They are grey in colour, more or less opaque, and, particularly when seated on the dura-mater, are often enclosed in a fibrous capsule.

Their cells are flat and thin, of colossal size and irregular form; they resemble a sail, and are often crumbled or folded over at the corner (A, fig. 73); viewed full face the border of the cell is so delicate that it is difficult to trace it; the centre is occupied by a lenticular nucleus; seen sideways it may be taken for a fibre, or an extremely long fusiform cell, the centre of which is filled with a nucleus. These elements so resemble the endothelial cells of the veins, that Robin looked upon angiolithic sarcoma as an epithelioma; as, however, the cells are not united together, they are deficient in the characteristic which we consider essential to the definition of epithelioma. These neoplasms are also sharply distinguished from all epithelial tumours by the fact that their

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blood-vessels are in direct relation with the cells, a condition which never exists in epithelial elements either in the physiological or pathological state.

The blood-vessels are numerous and easily isolated by dissociation; their walls, whatever be their thickness, are entirely composed of cells similar to those which constitute the whole morbid mass. The cells feebly adherent to one another are easily pushed aside by the blood current so as to form vessels.

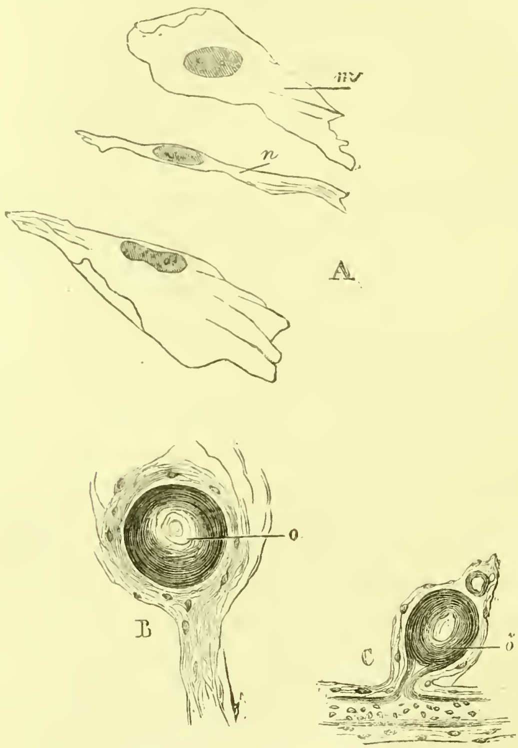

Fig. 73.—Angiolithic Sarcoma.

A, isolated cells seen full face at *m*, and sideways at *n*. Magnified 400 diameters. B, vascular bud containing a calcareous ball, *o*; C, blood-vessel infiltrated with calcareous salts, and showing at *o* a lateral bud infiltrated with calcareous salts. Magnified 150 diameters.

Hollow buds are often seen communicating with the vascular channel; these buds in growing become pedunculated, while the cellular elements which form the wall of the bud get flattened, arranged in concentric layers, and encrusted with calcareous salts. This process of infiltration is in every point similar to that which occurs in the choroid plexus. If these calcified buds have not lost their connection with the blood-vessel from which they spring, their pedicle and a part of the vascular branch, with which they are in connection, are often encrusted with calcareous salts to form a single mass (fig. 73); but if the pedicle be accidentally broken or be not infiltrated with calcareous salts, it may pass unperceived, the little round bud looking like one of the bird's-nest bodies of epithelioma. Virchow, who neither recognised the pedicle nor observed the process just described, looks upon these little buds as simple masses of cells, similar to bird's-nest bodies, and infiltrated towards the centre with calcareous salts. The fact, often easy of demonstration, that these balls are connected with blood-vessels alone differentiates them from epithelioma nests. They are not necessarily calcified though there is a strong tendency to calcareous infiltration; this property is again sufficient to distinguish them from epithelioma nests. In other parts of the body, particularly in the thymus, nests composed of concentric layers, calcified or not, are very frequently met with; these are also connected with vascular walls and have the same origin.

To recapitulate, although angiolithic sarcoma differs from the species already described by the form of its cells and the special modification of its blood-vessels, we think it allowable to treat it as a variety of sarcoma, inasmuch as it presents the same general arrangement of elements.

Myxo-sarcoma.—Mucoid degeneration of sarcoma cells, accompanied or not by fatty degeneration, ends in the destruction of the cells and the formation of cavities filled with a transparent gelatinous matter. These cavities vary greatly in size; they are often so large that they can hold an egg or a fist. The whole tumour may be riddled with them, in which case some authors call it cysto-sarcoma. The blood-vessels of mucous sarcomata generally show more or less considerable dilatations, and interstitial hæmorrhages may be concurrent; the extravasated blood, combining with the mucus, assists in forming the contents of a pseudo-cyst, and gives origin, according to the quantity present, to various tints, from red to chocolate brown, in proportion as the hæmoglobin is more or less abundant, or has undergone more or less complete change. The fibrin of the blood coagulates and also concurs in varying the appearance of the tumour. The cyst wall is not lined by epithelium; it is generally irregular and is not distinguishable by the naked eye, or by the microscope, from the rest of the tumour; it is sometimes covered by fibrinous lamellæ.

Very small parts of a sarcoma may be in a state of mucoid degeneration without it being permissible to call it a myxosarcoma. We only look upon sarcoma as mucous when the mucoid degeneration is very marked, almost general, and when it has attacked the most recently formed parts. Tumours of this kind may give origin to secondary tumours having the same degeneration. It is this fact which justifies the distinction of this variety of sarcoma.

Lipomatous sarcoma.—In this variety the sarcoma cells are infiltrated with fat without being destroyed or ceasing to live, a capital distinction which differentiates lipomatous sarcoma from that in which the cells are destroyed or are undergoing destruction from granular fatty degeneration. The cells of lipomatous sarcoma are large and fusiform ; those containing one or more fat droplets are naturally dilated, and the nucleus is pushed towards the periphery. The cells are close together and the ground substance is very slight in quantity. Owing to the presence of fat granules and the small quantity of ground substance, the tumour is sometimes so soft that surgeons are apt, at first sight, to call it encephaloid cancer, a mistake which would be impossible if the microscope were used. These tumours are generally very voluminous and may cause secondary growths.

Melanotic sarcoma.—Melanotic sarcoma has its usual point of origin in the eye or in the skin, but it may also appear primarily in the lymphatic glands. In a tumour in process of development not all the cells are pigmented nor equally so : zones may be observed of various colours which may be white, grey, often semi-transparent in the young parts, or black in the older parts and sepia or slate-coloured in the intermediate ones. Such is, in fact, the usual rule, but there are sarcomata which are entirely black from the beginning and throughout their entire mass. The cells are round or fusiform ; their arrangement and that of the intermediate substance vary, but in their form and grouping they recall that of fasciculated sarcoma (see fig. 74). The specific character of this variety of tumour is the presence of black granules in the interior of its cells. These granules are never yellow or reddish when they first appear, a fact which establishes a fundamental distinction between melanotic black pigment and the black pigment present after extravasation of blood. When blood is infused into cellular tissue, the colouring matter of the blood infiltrates the cells—the epithelial cells of the lung in pulmonary hæmorrhage for example—and the colouring matter is deposited in the form of yellowish-red pigment, which turns first red then black: the whole series of these changes may be followed as Virchow has shown. In melanotic sarcoma, however, the granules are colourless, grey or black from the beginning, and are round and highly refractive; at first they might be confounded with very fine fat granules, but when angular they are more easily recognised; they are often aggregated together into small round blocks surrounded by a clear zone corresponding to a deposit of albuminoid material around them. If the black juice obtained by scraping be examined, a great number of these granules are seen floating free in the fluid and agitated by Brownian movements. Melanotic granules are first deposited in the protoplasm surrounding the nucleus, subsequently in the whole cell. The ground substance is also soon pigmented and often more strongly so than the cells, while the nuclei themselves may be infiltrated with melanin, in which case they are more or less strongly tinted. On adding acetic acid they contract and become darker, almost black.

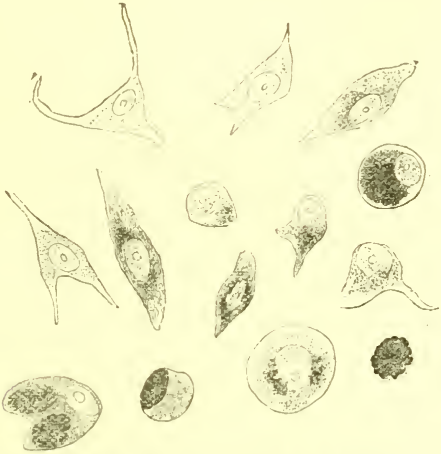

FIG. 74.—VARIOUS FORMS OF CELLS FROM A MELANOTIC SARCOMA.

This form of sarcoma is well marked and distinct from the other forms by the tendency its elements show to become completely black, and by the same tendency in secondary products originating far from the primary tumour. Secondary growths, in the form of nuclei and black masses, are formed in great rapidity and may be found in all the organs and tissues of the economy. Melanotic sarcoma must not be confounded with simple melanosis, which may also take the form of tumours (see the description of simple melanosis, given elsewhere). It is not always easy to distinguish melanotic sarcoma from melanotic carcinoma. Melanotic tumours of the skin and of the subcutaneous cellular tissue are often of such a structure that hesitation must be felt before deciding whether the case be one of sarcoma or carcinoma. Clinically, this is not of much importance, since the prognosis of all tumours of the kind, whether sarcoma or carcinoma, is extremely grave. The name of melanotic sarcoma must not be given to those tumours in which extravasation of blood has occurred, producing little brown or slate-coloured masses. This is an accident which may be observed in different varieties of sarcoma, and which does not constitute a distinct species. Melanotic sarcoma is very common in white horses, in which animals it is rapidly propagated in all the organs.

Papillary sarcoma.—The different species of sarcoma described above take the papillary form when seated in a mucous membrane or the skin. We have already indicated that sarcoma of the breast has a tendency to bud into the interior of the acini and galactophorous ducts. Sarcoma of the skin sometimes shows on its surface rugæ, and irregular projections bounded by depressions, at others it is decidedly of the papillary and budding variety. In consequence of the proliferation of their cells, the papillæ of the corium undergo considerable hypertrophy and lateral buds may even be given off. They are covered by epidermic layers, the cells of which are more pigmented than normally. In certain cases, even the cells of sarcomatous papillæ are also slightly pigmented ; it is possible that here may be the beginning of a melanotic sarcoma, but in the majority of cases the pigmentation seems to be due to ecchymoses. The cells of these papillary buds are often voluminous and pressed one against the other, so that if but little ground substance be present they may become polygonal in form. Large mother-cells (*myéloplaxes*) are also found here. The very numerous blood-vessels are in immediate relation with the cellular elements of the new tissue. These tumours grow rather slowly, but they may, however, at a given moment increase rapidly and cause secondary growths.

Development, extension, and generalisation of sarcoma.—The development of sarcoma, like that of most tumours, has three stages : 1, the development of the primary tumour ; 2, the growth of the primary tumour ; 3, the formation of secondary tumours.

I. The development of the primary tumour is very simple. It were well if it were possible to examine the neoplasm from its first appearance, but this is not absolutely necessary, for the process of growth may be studied in the peripheral parts of the tumour, hence it is only necessary that the tumour should show parts in course of formation, a condition which is however not always present. Development should also be studied by preference in tissues of which the structure differs greatly from that of the sarcoma, in order to mark and follow the series of striking changes. In bone, the development of sarcoma is exactly similar to that of inflamed tissue; the proliferation of the medulla-cells, the disappearance of the fat vesicles, and the consecutive absorption of the osseous tissue, are identical, and we shall therefore not redescribe them (see page 92). In tendons, the connective-tissue cells, atrophied in the adult condition, swell, their nuclei divide, are separately surrounded by distinct masses of protoplasm, and the new embryonic cells are arranged in long lines whilst the fibrillar substance disappears. Hence results an embryonic tissue similar to that of encephaloid sarcoma, but which may become, by changes in its cells and ground substance, a fasciculated sarcoma, an osteoid, &c. This type of development is found in areolar connective tissue, in cellulo-adipose tissue, &c; it is not necessary to insist here more upon it. It is only necessary to recall the fact, that in every case of sarcoma, the adipose tissue disappears, the cellulo-adipose subcutaneous tissue as well as that in the breast.

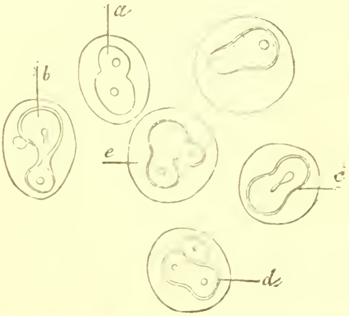

FIG. 75.—VARIOUS PHASES IN THE DIVISION OF THE NUCLEOLUS AND NUCLEUS OF CELLS TAKEN FROM SARCOMA OF A HORSE.

a, nucleus restricted and showing two nucleoli; *b*, division more advanced; *c*, nucleolus undergoing division; *d*, *e*, various forms of segmentation of the nucleus. Magnified 450 diameters.

II. The growth of the primary tumour takes place—(*a*) *By proliferation of its own cellular elements.* The cells multiply by division, which begins with the nucleus, and is soon followed by that of the cell. In sarcoma all the phases of cell multiplication by division may be followed; a nucleus in the form of an hour-glass or presenting more or less deep notches, two or a great number of nuclei in the same cell, two cells united by a thin process,—these all may be observed. The prognosis of tumours which develop by proliferation of their own cells is less serious than by the two following modes: (*b*) *By continuous invasion of neighbouring tissues.* If the excised morbid mass be smooth and uniform at its periphery, it signifies that it has not invaded the neighbouring tissues. If not sharply bounded, but melting gradually into the surrounding parts, it shows that the neoplasm is invading the neighbouring tissues. This may be proved by microscopic examination of the peripheral regions, where masses of embryonic tissue may be found in course of formation at the expense of the normal elements of the tissues. (*c*) *By interrupted or discontinuous invasion.* The preceding mode gives ground for a serious prognosis, but less serious than when morbid masses, isolated from the principal tumour, are met with in the surrounding regions; this is called discontinuous invasion, and when found it may be suspected that similar growths exist near the primary tumour in parts not excised by the surgeon. In this case secondary growths *in situ* and in distant organs may be feared.

III. When new tumours of the same nature as the primary growths are developed in distant organs there is said to be *generalisation*; this is also called *metastasis*, from a pathogenic idea not yet proved. We have based our classification of sarcoma on the property which the various species admitted by us possess of reproducing themselves with their specific characters in secondary tumours. Thus, secondary masses arising from the generalisation of encephaloid, melanotic, and mucous sarcoma, &c., possess a structure essentially similar to that of the primary tumour.

Prognosis of sarcoma.—The gravity or malignity of sarcoma depends particularly on the energy of its progressive development, continuous or discontinuous, and on its generalisation. Every voluminous tumour is serious, but besides the gravity due to its volume, sarcoma often extends to neighbouring parts and frequently relapses locally after ablation; sarcomata moreover, with the exception of the angiolithic and neurogliac varieties, have a tendency to generalisation. The gravity of sarcoma, however, is relative and varies according to the species. It may be said that a sarcoma is more serious the lower is its organisation, or in other terms that sarcoma, formed solely or for the most part of embryonic elements, is much more serious than that in which these same elements show a tendency to become organised into connective tissue, bone, &c. Thus, in order of gravity, the classification of sarcomata should be: encephaloid, melanotic, colloid, lipomatous, and then fasciculated and ossifying sarcoma. The sarcoma which shows veritable osseous trabeculæ is less to be feared than that which has simply undergone calcification. The more marked the tendency of the sarcoma to produce perfect tissue and the more advanced the organisation, the less serious is the sarcoma. Thus amongst myeloid sarcomata, those which most resemble the medulla of bone are more benign than those in which parts are found representing the tissue of encephaloid or fasciculated sarcoma. It is essential to take note of these complications, they are of great prognostic value, and explain why tumours which some authors still call 'tumours of myeloplates' cannot always be regarded as benign. Virchow, who has made no distinction between ossifying and calcifying sarcoma, says that in a general manner they are both serious; but by differentiating one from the other, we are enabled, on the contrary, to say that ossifying tumours, such as epules or subungueal tumours, are, as everybody knows, benign, while fasciculated sarcoma encrusted with calcareous salts is grave, the gravity resulting, not from calcification, but from its species as a fasciculated sarcoma. Neurogliac sarcoma is grave, by reason of its situation and the extension of the primary tumour, but it never becomes generalised. The same may be said of angiolithic sarcoma, which has no tendency to generalisation, and less than the preceding to extend and become voluminous; it very rarely causes symptoms by which it may be recognised during life, and is found by chance in persons dead of another disease.

To recapitulate what we have stated with regard to the diagnosis and prognosis of sarcoma, we may say—I. That it is essential first to determine to which genus, species, and variety of sarcoma the tumour examined belongs. II. That the prognosis of sarcoma must be deduced, first from its classification in respect to its species, secondly from its mode of development, continuous or discontinuous, and finally from the presence, in more or less considerable quantity, of new embryonic elements in its neighbourhood. From what precedes it is evident that, at the present day, the mode of investigating tumours is more precise than at the time when it was thought sufficient to scrape the surface of the section of a tumour and to look for specific cells. All the preceding ideas of genus, species, variety, and mode of development, are essential to enable the surgeon to establish the diagnosis and prognosis of the tumour he is about to remove.

II.—TUMOURS THE TYPE OF WHICH IS FOUND IN THE DIFFERENT VARIETIES OF CONNECTIVE TISSUE.

CLASS I.—Myxoma.

Definition.—Myxoma is a tumour composed of mucous tissue. Its definition is given by that of the mucous tissue itself. This tissue forms the umbilical cord ; in the adult it is only persistent in the vitreous humour of the eye, but in the embryo is found in various parts of the body. In the embryo, mucous tissue is observed as one of the earliest phases in the development of connective and adipose tissue, so that tumours formed of it have consequently their place indicated for them between the sarcomata, formed of embryonic connective tissue, and tumours composed of perfect connective tissue. Physiologically, mucous tissue presents two varieties : 1, isolated round cells in the midst of a mucous ground substance ; 2, stellate and anastomosing cells arranged in the midst of the same substance. It is rare for myxoma to be composed solely of one or the other of these varieties, while we have never observed a tumour composed only of the first variety.

Description of myxoma.—Myxoma is a gelatinous, mucous tumour, traversed by blood-vessels which are easily recognised and isolated. On scraping, a fluid is obtained resembling a solution of gum arabic—milky juice is never found. In this fluid red corpuscles are found, owing to the contents of a number of divided blood-vessels having been squeezed out, and also cells of various shape, round, angular, or fusiform, many with processes. They contain one or many nuclei, and are all pale with ill-defined borders, since they are seen in a substance almost as refractive as themselves. Hence the old opinion that myxoma had no cellular elements.

The tissue may be studied in the fresh state. After section of the tumour, the divided surface swells in a ridge-like manner ; this may be sliced off by a second section and the raised part, though thick in the centre, is sufficiently fine at the borders to be examined microscopically. In a preparation thus made, a large meshed network of capillary vessels containing red corpuscles is first perceived; the nuclei of the walls and even the endothelial cells of the internal coat can be easily made out; between the vascular meshes is seen the mucous tissue, containing large, pale cells, fusiform or anastomosing by numerous processes. Besides this cellular network there are always small, round cells, unconnected with neighbouring cells, suspended in the mucous fluid. This network of cells is rendered more apparent by the addition of a solution of iodine, or of picro-carminate of ammonia. Besides these elements, elastic fibres and fat cells are often met with. Such are the general characteristics of tumours of this class.

Species and varieties of myxoma.—I. *Pure myxoma* is composed of blood-vessels and of a mucous material, in which are distributed round or stellate cells more or less large.

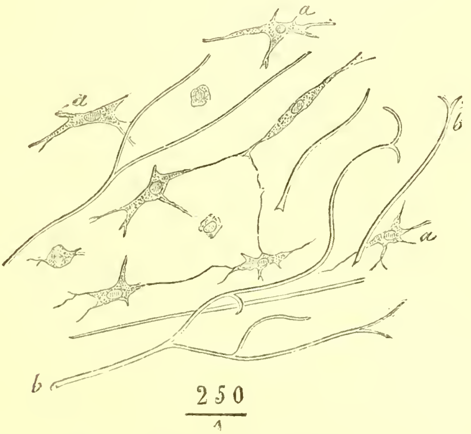

Fig. 76.—Section of Myxoma containing Elastic Fibres.

a, stellate and anastomosing cells; *b*, elastic fibres.

II. *Myxoma containing a considerable quantity of elastic fibres* (fig. 76).

III. *Lipomatous Myxoma.*—In the midst of the mucous tissue fat cells, isolated or massed together, are often so abundant that it is frequently embarrassing to decide whether we have to do with a myxoma or a lipoma. The distinction is however almost useless, for myxomatous lipoma and pure lipoma closely resemble each other from the histological point of view and are equally benign (fig. 77).

Besides these three species which define themselves and require no more detailed description, myxoma often undergoes the following nutritive changes:—

a. The blood-vessels, ill supported by an almost fluid tissue, may become distended and ruptured—an accident less frequent than in sarcoma, for the capillary walls are comparatively more solid. This accident characterises *telangiectasic* and *hæmorrhagic myxoma.*

b. The cellular elements of the tumour often undergo mucoid or colloid degeneration, which may at first sight seem surprising, seeing that myxoma is essentially mucoid. But it must not be forgotten, that in true myxoma the intercellular substance alone is mucous and that the cells suspended in it are ordinary connective-tissue cells. They are not flat, for being immersed in a fluid mass they have equal pressure on all sides; they are composed of a mass of active protoplasm, contain one or more nuclei, and are subject to mucoid or colloid degeneration, like many other cellular elements; when undergoing mucoid degeneration, they break down, forming a detritus, and in their place is left a mucous mass contained in a pseudo-cyst. Vascular ruptures frequently occur, and to the substance contained in the cysts is added blood which undergoes the usual retrogressive changes. Colloid degeneration of myxoma cells is generally accompanied with fatty degeneration, which aids in bringing about their death. When pseudo-cysts are formed in myxomata in consequence of degeneration or hæmorrhage, the colour and consistency of the morbid mass vary so greatly, that the diagnosis cannot be made without the aid of the microscope. This variety of myxoma may be called *cystic myxoma.*

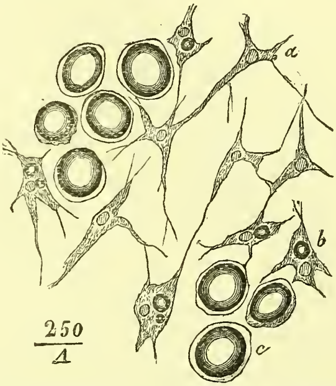

FIG. 77.—SECTION OF LIPOMATOUS MYXOMA.

Cells of the mucous tissue filled with fat; *a*, normal cell; *b*, cell containing a drop of fat; *c*, cell quite full. Magnified 250 diameters.

c. Myxomata of the mucous membrane are often papillary, pedunculated, or polypoid. Such is myxoma of the nasal fossæ, known under the name of *mucous polypus*. This form of polypus, developed from the cellular-tissue of the pituitary mucous membrane, is covered by the cylindrical, ciliated cells of this membrane. When projecting externally, it often presents at certain points more or less hypertrophied glandular tubes. The mucous tissue of nasal polypus is very subject to fatty degeneration and to interstitial hæmorrhage. A most singular variety of papillary myxoma is seen in the *hydatid mole* or *hydatiform myxoma of the placenta*. These moles are formed of round or pyriform masses of mucous tissue (fig. 78), varying in size, and bound together in great numbers by portions of the placental villi which have not undergone myxomatous change. When these moles have attained a certain size they usually undergo fatty degeneration and become opaque. Interstitial hæmorrhage is sometimes observed in them.

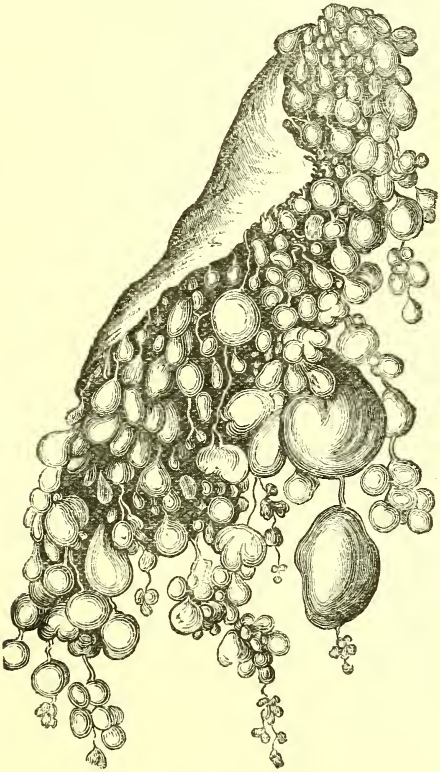

FIG. 78.—HYDATIFORM MYXOMA OF THE PLACENTA.

Figure borrowed from Virchow's 'Pathology of Tumours,' and enlarged.

d. When myxoma is superficial, especially if of the polypoid variety, it may inflame and ulcerate. Embryonic and pus cells are then developed in large numbers in the same way as in all inflamed tissue.

e. Myxoma may also become gangrenous in its entirety or in part.

The **seat of myxoma** is variable. It sometimes develops, as we have just seen, in the *placenta*, forming the hydatiform mole of that organ. In the *umbilical cord* of the embryo or new-born infant, small ill-defined myxomatous growths are met with, forming slight projections on the surface of the cord. The name of myxoma should, however, hardly be applied to these, though nevertheless they must be so called, for they are sometimes found the size of a pigeon's egg. Myxoma is rather frequent in the *subcutaneous cellular tissue.* It also invades the *muscles*, where it is developed from the connective tissue situated between the muscular fasciculi; the latter, separated from one another by the morbid neoplasm, become slowly atrophied, a change which is indeed generally observed in cases of invasion of striated muscle by tumours. The primitive bundles show a multiplication of their nuclei and undergo fatty degeneration; they become thinner at various points and may be separated into little fusiform blocks

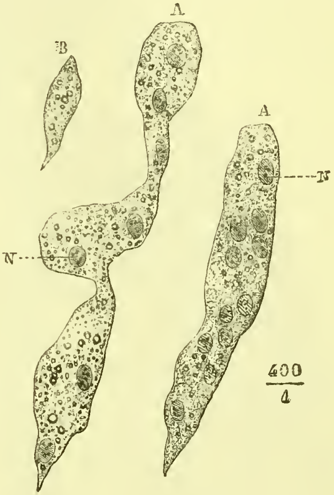

Fig. 79.—Much Atrophied Muscular Fasciculi obtained by Dissociation of a Myxoma developed in the Masseter Muscle.

A, A, primitive bundles containing nuclei, *n*; B, a fasciculus in the last stage of atrophy.

pointed at the two ends (A, B, fig. 79); these are sometimes isolated, or they may be united by delicate filaments which represent the empty and collapsed tubes of sarcolemma. In *nerves* myxoma is frequent; it is then generally called *neuroma*, owing to a confusion which it is important to avoid, for to be consistent in our classification we give the name of neuroma only to tumours formed of nervous tissue of new formation. In myxoma of the nerves, the nervous fasciculi are generally dissociated and spread out on the surface of the tumour (B, fig. 80), which therefore occupies the centre of the nerve; but it is not always so, for the nerve tubes may be found in the centre of the morbid mass. The power of resistance which the peripheral nerve tubes offer to the compression and invasion of these tumours is truly remarkable. They do not generally undergo any appreciable

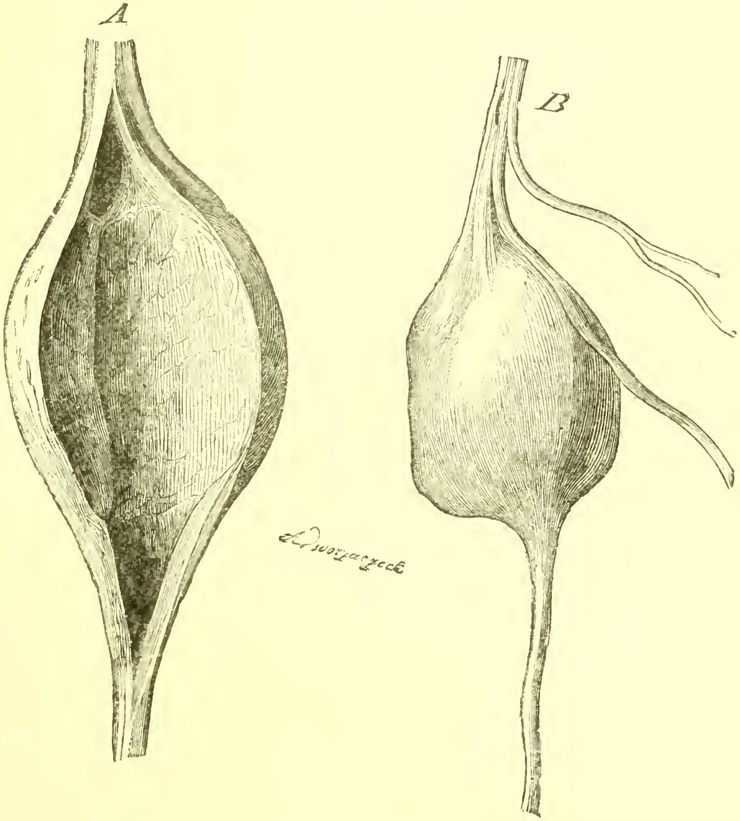

FIG. 80.—MYXOMA OF NERVES.

nutritive change. This peculiarity is, however, in agreement with what we know of the resisting power of nerves to all neoplasms. In the *brain* myxoma forms a greenish-coloured tumour (*collonema* of J. Müller). The *glands* may also be the seat of myxoma. It has been observed in the papillæ of the *kidney*. In the *mamma* myxoma is rather common; like sarcoma of the mamma, it is seen under various forms. It may consist of a more or less defined mass in the midst of which a number of acini are generally found, the epithelial cells of which are hypertrophied and proliferating. It may, like sarcoma, take the papillary and budding form; the myxomatous tissue then projects into the interior of the galactophorous ducts and acini and spreads by budding. The buds are variable in number, may be of a considerable size, and, by distending the glandular cavity in which they are contained, may transform it into a lacunar cavity, often of great size. These lacunar cavities are lined with pavement or cylindrical epithelium. Care must be taken not to confound such a tumour of the breast with adenoma. This is an error all the more easy to fall into, inasmuch as the proliferation of the epithelial cells of the glandular ducts and the different changes of the papillæ and buds, indicated above, may at first sight give rise to the opinion that the tumour is a cystic adenoma. The anatomical diagnosis depends upon the tissue situated between the glandular elements. We have often witnessed singular mistakes made in the diagnosis of papillary and cystic myxoma of the breast; numerous and complicated growths projecting into dilated glandular ducts have been taken in our presence, even by well-trained histologists, for glandular acini. By superficial observation, however, it may be ascertained that the growths are lined by epithelial and not by glandular cells. Myxoma may be seated under the periosteum, forming a lobular tumour; it is also met with in *bone*, particularly in the short bones, when it is generally well defined and springs from the periosteum; it has, however, been seen to develop in the interior of spongy tissue. In the *skin* myxoma often takes a papillary form.

Anatomical diagnosis of myxoma.—Differential anatomical diagnosis only leads to confusion if an attempt be made to determine whether a tumour be sarcoma with mucoid degeneration, or myxoma with spots of embryonic tissue. But this source of error may be avoided by remembering that at the spots where sarcoma is undergoing mucoid degeneration, the cells are destroyed, while in the remainder of the tumour the proper structure of sarcoma is preserved. The presence of elastic fibres or true adipose cells immediately suggests myxoma.

Prognosis of myxoma.—Myxoma is not usually very serious. If completely removed it rarely recurs. If incompletely extirpated, as may happen, particularly in soft polypus situated high up in the nasal fossæ, it redevelops with new vigour like every other tumour irritated by surgical interference which has not been successful. The continuous growth of myxoma takes place at the expense of the neighbouring connective tissue which becomes embryonic, or at the expense of its own mass. In fact, nests of embryonic tissue are sometimes found in the centre of the tumour, and it is possible that this new formation takes place by hyperplasia of the cells of the mucous tissue. Virchow has often seen myxoma become generalised, and it is probable that the tumour is the more serious the more embryonic tissue it contains, and the more benign the more elastic and adipose tissue.

Class II. Fibroma.

Synonyms.—This tumour has also received the name of *fibroid* or *desmoid.* If very hard J. Müller called it *steatoma*, a vague name applied to many different species. It has also been called a *fibroid body*, but this expression has been chiefly applied to tumours formed of unstriped muscular fibres, which consequently are myomata. Verneuil proposed the name of *fibroma*, which is that generally employed and which defines the tissue, though the the word *inoma*, used by Paget and formed from the Greek radicle (*ινος*, fibre), may be preferable in the opinion of a purist.

Definition.—The definition of fibroma is supplied by that of fibrous tissue, composed, as is well known, of bundles of connective tissue separated by flattened connective-tissue cells, ramifying and anastomosing with one another. There is also another special form of connective tissue composed of fibrillar lamellæ, between which are flat connective-tissue cells; this form is met with in the internal coat of large arteries and in the cornea. Both these varieties of connective tissue may be seen in fibroma. For a tumour to be called fibroma it is not enough that it should contain connective tissue, it must also contain no other tissue. Nearly all tumours have a fibrous framework. Carcinoma, for example, has a fibrous stroma often dense and predominating in certain parts of the tumour, but it always limits alveoli filled with cells; tumours consisting of cellulo-adipose tissue also often contain much fibrous tissue surrounding islets of fat cells ; in most sarcomata and myxomata, there are near the tumour and sometimes within it fibrous tracts which generally accompany the large vessels. But in these various tumours the fibrous tissue only constitutes the framework supporting the most characteristic parts of the neoplasm. Fibroma on the contrary is composed solely of connective tissue.

Description of fibroma.—Fibroma is a dry, resisting, pearly, rose-coloured or whitish tumour. If after division the surface be scraped with a razor no juice is obtained, but small portions are detached, which, if examined in water, seem to be entirely formed of rectilinear or undulating connective-tissue bundles ; if acetic acid be added they are changed into a homogeneous mass, in the midst of which nuclei are apparent ; but the cells, to which these nuclei belong, are somewhat difficult to isolate. They are connective-tissue cells differing little from those of myxoma.

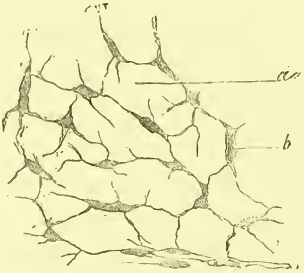

FIG. 81.—SECTION OF FIBROMA, STAINED WITH CARMINE AND TREATED WITH ACETIC ACID.

a, bundles of fibres cut across ; *b*, anastomosing connective-tissue cells. Magnified 200 diameters.

Connective-tissue fibres being met with in all tumours, dissociation does not give sufficient data on which to make the diagnosis ; in fact, with regard to the differential diagnosis between carcinoma and fibroma (see later), dissociation may lead to error, as portions of hard or scirrhous carcinoma are solely formed of fibrous tissue. Sections should therefore be made of the morbid mass after hardening with alcohol, chromic acid, picric acid, gum and alcohol, or after simple dessication. Examination will then easily permit the observer to ascertain if, in the midst of the fibrous tissue, the alveoli of carcinoma, epithelial islets or unstriped muscle fibres, &c. are present. In a fine section of a fibrous tumour, bundles of fibres are seen crossing one another in various directions, as in the skin, some in a longitudinal, others in a transverse direction.

The arrangement of these bundles can be well seen if the preparations are examined in water, not so well if they are preserved in glycerine, and is hardly perceptible at all if acetic acid be added. The last reagent makes the nuclei apparent and of a red colour, if care be taken to previously stain the section with carmine; the nuclei and the cellular bodies surrounding them are then clearly seen to be arranged around the longitudinal or transverse bundles (see fig. 81). There are generally no elastic fibres in fibroma, the tissue appearing to be the purest form of fibrous tissue. This is an important point. The vessels are not abundant, and are even wanting in the species called lamellar fibroma.

There are two species of fibroma: 1. **Lamellar fibroma**; 2. **Fasciculated fibroma.**

I. Lamellar fibroma.—On serous membranes such as the pleura, pericardium, and peritoneum—particularly that fold of the peritoneum which covers the liver and more especially the spleen—hard tumours are often seen arranged in plates, villosities, or little globular masses. They are included by certain authors in the description of chronic peri-hepatitis and peri-splenitis. These tumours are more or less thick and are sometimes flattened on the convex surface of the organ, so that on being divided perpendicularly they appear crescentic in shape; at other times they are projecting and form one or many lobules united by fasciculated connective tissue. These bodies have a coarse analogy to cartilage. They are translucid, slightly yellow, hard and difficult to cut, resisting under the scalpel, but do not creak like cartilage when cut. The arrangement of the concentric or parallel layers of which they are composed is easily seen with the naked eye; it is this arrangement in flattened lamellæ which gives them the feel of extreme hardness when subjected to pressure perpendicular to their surface, while on pressing them laterally they are found to be relatively

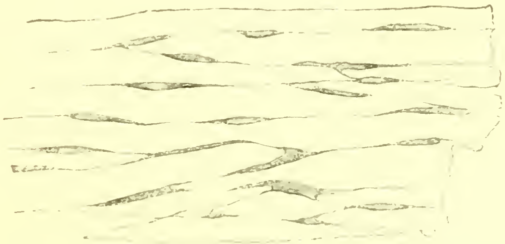

FIG. 82.—TRANSVERSE SECTION OF A LAMELLAR FIBROMA.

soft. They are hard enough to admit of delicate sections being made in the fresh state. These when examined under water, without the addition of any reagent, show parallel lamellæ separated by openings, resembling the layers of fibrin lining an aneurismal sac. After staining with carmine and being submitted to the action of a mixture of glycerine and formic acid, well-defined cells with flat nuclei and united together by ramifying processes are seen to occupy the openings. These preparations so closely resemble those of sections of the cornea perpendicular to its surface and stained in the same manner, that Rindfleisch has called this tumour *corneal fibroma*. It contains no blood-vessels. Calcareous infiltration is frequent; fine calcareous granules are deposited in the ground substance, where they are at first isolated, then united into groups; the tissue now becomes opaque, yellow, and solid, while the granules increase in size, join together, and bring about a true petrifaction. Hard and transparent plates of variable size are thus produced; the whole fibroma may undergo similar transformation, but more frequently many superimposed calcareous lamellæ can be distinguished, separated from one another by non-calcified fibrous tissue, while at the periphery of the indurated plate distinct calcareous granules are almost constantly met with. Such are the petrified growths which the old writers on pathological anatomy called by the name of osseous plates of the pleura, peritoneum, &c. Calcareous degeneration in these tumours almost always begins in the cèntre of each lobule.

II. **Fasciculated fibroma.**—To the naked eye this fibroma has a characteristic appearance; it is formed of a conglomeration of lobules, each composed of a ball of fibres. On section of the tumour the centre of each lobule projects. Many similar lobules are united together by loose connective tissue traversed by blood-vessels which penetrate sometimes, but not always, into the interior of the lobules. This fibroma is formed of bundles of connective tissue intersecting in every direction and leaving interfascicular spaces in which cells similar to those of young or adult connective tissue are found (see fig. 81).

The varieties of fasciculated fibroma depend upon some modifications of nutrition; they are as follows:—

a. **Mulluscoid fibroma** or **Molluscum simplex.**—In this variety there is serous infiltration as in œdema; the connective-tissue bundles remain perfectly distinct, but are infiltrated with serous fluid.

b. **Mucoid fibroma.**—Here mucoid degeneration of the fibres and cells has taken place leading to partial destruction of the tumour and the formation of a pseudo-cyst.

c. *Fatty degeneration* is rare in fibroma with the exception of those of syphilitic origin. In conjunction with mucoid degeneration it attacks the centre of syphilitic fibromata ; it may disappear in the natural progress of the disease or as the result of treatment.

d. *Calcareous degeneration* is so frequent in fibroma that few cases of fibroma are free from it, if they have existed a long time. It begins at the centre of the lobules, that is at the points furthest removed from the blood-vessels. Virchow admits varieties of fibroma according as it enters into combination with lipoma, myxoma, and carcinoma. It is clear that fibrous tissue is always met with in these tumours as an accessory element, and there is nothing essentially novel in their constitution when this tissue exists in greater or less abundance. They are none the less lipoma, myxoma, or carcinoma.

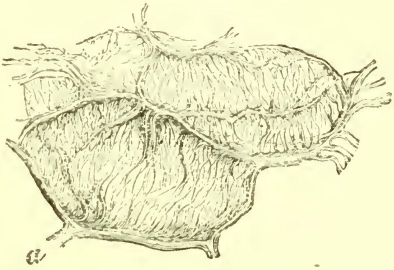

FIG. 83.—MOLLUSCOID FIBROMA OR MOLLUSCUM SIMPLEX.
Figure borrowed from Virchow's 'Pathology of Tumours.'

e. *Inflammation* occurs when fibroma takes the form of a projecting polypus. When irritated by contact with neighbouring solid or fluid parts it may inflame, ulcerate, and granulate, like other suppurating wounds. New embryonic elements are developed in the parent mass from the older cells, while the dissociated fibres are destroyed ; in a word, the same phenomena of inflammation occur as in normal connective tissue.

The **development of fasciculated fibroma** is not well understood, for these tumours are generally removed when growth is stationary or completed. We have not studied the subject from personal observation, but Förster has noted islets of embryonic tissue in growing fibroma, from which it would seem that each constituent lobule has a distinct, autogenic development.

The **seat of fibromata** is variable. In the *skin* they are generally projecting in the form of hard moles or polypi. *True molluscum* is also met with in the skin (we do not mean *molluscum contagiosum* formed by the sebaceous glands and called by Bazin *varioliform acne*), and is included by some writers among fibromata. A series of lobules are found here, less defined than in other fibromata, for the whole tissue is soft. The tumours are sometimes solitary and small, and sometimes of such an enormous size that they have been known to weigh fifteen to twenty pounds. Undulating bundles of connective tissue are found in islets, saturated with serum (fig. 83), while a large quantity of fluid is present between them. Surrounding the bundles, cells are observed, and if the development of the tumour is active, embryonic or migratory cells are found. Molluscum is vascular throughout.

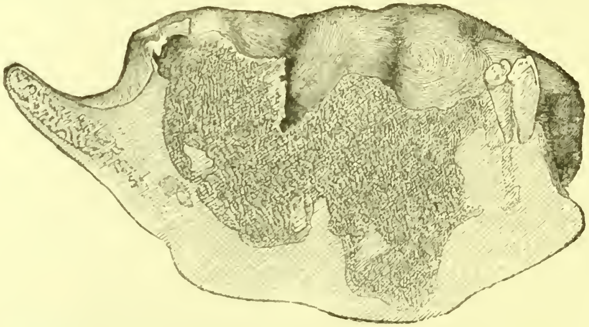

FIG. 84.—CALCIFIED FIBROMA OF THE MAXILLARY SINUS.
Figure borrowed from Virchow's 'Pathology of Tumours.'

In the subcutaneous cellulo-adipose tissue, particularly on the internal surface of the tibia, very dense and small fibromata are met with, varying in size from that of a millet seed to that of a pea. In the same subject, they may be found at different periods of evolution and calcareous infiltration, petrified only at their centre or throughout the whole mass. They are generally encysted and surrounded by a true serous bursa, and though often attached to the cyst-wall by a more or less lengthened pedicle they are mobile under the skin. Fibroma of the *mucous membranes* is rare; less frequent in this position than myxomata or tumours formed of unstriped muscular fibres. In the *breast* fibroma shows itself under two forms. It may be a homogeneous mass and correspond to the description given of fasciculated fibroma (the *fibroid body* of the breast of Cruveilhier), or it may be complex and accompanied by proliferation of the epithelium lining the acini and ducts of the glands. The galactophorous ducts increase in size and are transformed into true lacunar cavities, into which fibrous and generally vascular growths project (*b*, fig. 85), these growths being lined with epithelium (see *c*, fig. 86). In the *periosteum* fibroma is frequent. With regard to the differential anatomical diagnosis between fibroma and sarcoma of the periosteum, Virchow insists that fibroma does not invade bone like sarcoma. Fibroma is, in fact, always distinct from neighbouring tissues, while sarcoma is surrounded by an invading peripheral layer of embryonic tissue. Retro-pharyngeal polypus is generally a fibroma developed in the periosteum of the bones at the base of the skull. Virchow describes small fibromata of the *kidney* situated at the union of the cortical and medullary substance, but as interstitial nephritis is always present in such cases these are no more fibromata than those collections of fibrous tissue which are always found in cirrhosis of the liver.

Prognosis of fibroma.—Fibroma is benign and generally solitary. It does not relapse after removal, though retro-pharyngeal fibroma seems to be an exception to the rule ; this form of fibroma certainly relapses frequently, but to establish the gravity of the species we must be sure that the whole tumour has been removed, and that the anatomical diagnosis has been correct. Molluscum is sometimes serious by reason of its extension to a great number of spots on the skin, or of its great size. We may say, however, that all things being equal, fibroma is less serious than myxoma ; this is comprehensible as mucous tissue is more nearly allied to the embryonic type than fibrous tissue.

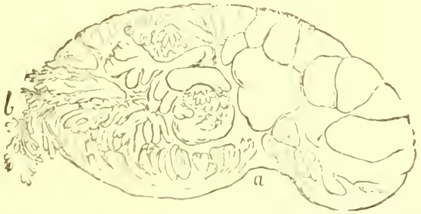

Fig. 85.—Lacunar Fibroma of the Breast.
Figure borrowed from Virchow's 'Pathology of Tumours.'

The anatomical diagnosis of fibroma is easy. The cystic variety of sarcoma and myxoma is the sole form of tumour which may be confounded with certain mucous fibromata ; but data for solution of the problem are always to be found in the periphery of the cysts.

Class III. Lipoma.

Synonyms.—Cruveilhier proposed the name of *adipoma* for this tumour, but it is not so good as that of lipoma, for the radicle is latin. When a lipoma was firm it was formerly called *steatoma*. Cruveilhier also called it *adipo-fibroma*.

Definition.—The definition of lipoma is given by that of the cellulo-adipose tissue of which it is composed. Normally cellulo-adipose tissue is formed of vesicles which are spherical, or polygonal from reciprocal pressure, the vesicles resulting from the accumulation of fat in embryonic or connective-tissue cells, the nuclei of which are pushed towards the periphery. The adipose vesicles are contained in a network of capillaries, and form little groups separated from one another by fibres of connective tissue. Every circumscribed collection of adipose tissue is not necessarily a lipoma. The mass of adipose tissue which replaces an atrophied organ, or the presence of a large quantity of adipose tissue in the great omentum or other parts of corpulent subjects, does not constitute lipoma. This name must be reserved for circumscribed masses of adipose tissue having, up to a certain point, a vitality independent of that of the rest of the organism. This independent vitality is demonstrated by the fact that an individual affected with lipoma may emaciate without the tumour diminishing in size, which is not the case with other adipose deposits.

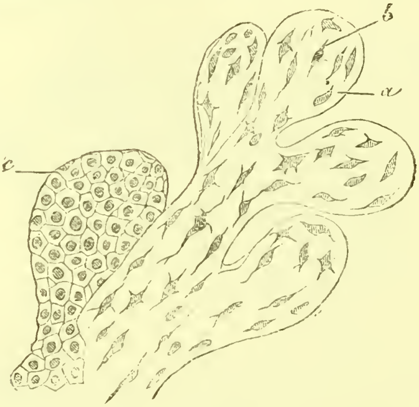

FIG. 86.—PAPILLARY FIBROMA OF THE BREAST.

Fibrous vegetations projecting into the galactophorous ducts which have become cystic; they are lined by epithelium at *c*, and denuded of it at *a*; *b*, connective-tissue cells. Magnified 300 diameters.

Description of lipoma.—Physiologically, adipose cells are grouped together to form lobules of fat. These lobules are also met with in lipoma. The adipose vesicles are large and surrounded by a cell wall which is easily seen; the nucleus is also distinct. The lobules are larger than normal, and to this peculiarity of structure is due the feeling of softness and false fluctuation which is characteristic. The appearance of lipoma and its complete resemblance to subcutaneous cellular tissue renders the employment of the microscope for its recognition rarely necessary. Microscopical examination is only useful to ascertain certain forms or varieties of lipoma, and certain modifications of nutrition, which it sometimes undergoes. Lipoma varies in size from that of a cherry to those colossal dimensions which make this tumour the heaviest which afflicts the human species. Lipoma may be lobulated, diffuse, or distinctly defined; it may be found in the form of polypus, solitary or multiple. Weber has counted 200 on the same subject, and there are similar observations which suggest the idea of a lipomatous diathesis.

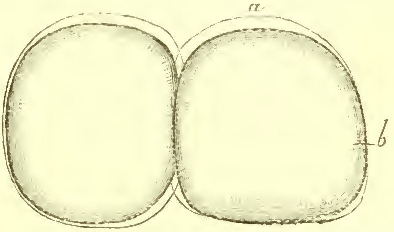

FIG. 87.—ADIPOSE VESICLES FROM A LIPOMA.
a, cell wall; *b*, fat drop. Magnified 300 diameters.

With regard to the **seat of lipoma** it is frequently observed in the *areolar tissue of the skin*, where it is often pedunculated. In the subcutaneous cellular tissue it is capable, in certain regions, of becoming displaced by its own weight; a lipoma is said to have been seen to descend, under the skin, from the umbilicus to the perineum, its form being preserved. In the *stomach* and *intestines* pedunculated lipomata have been seen to project into the cavity of these viscera. As cellulo-adipose tissue does not exist normally in the sub-mucous tissue of these cavities, lipomata must here be regarded as heteroplastic—an example of the inanity of the idea that heteroplastic tumours are synonymous with malignant tumours. Certain serous membranes normally possess villous growths composed of adipose tissue, such as the *appendices epiploicæ* of the large intestine, which may hypertrophy, become detached and fall into the peritoneal cavity, where as we have said above they undergo fatty or calcareous degeneration; such are also the *synovial fringes* which may likewise become lipomatous (the arborescent lipoma of O. Weber). In *muscles*, fat cells are grouped parallel to the muscular fasciculi, and may become the seat of lipoma. The muscular fasciculi remain normal, which is not generally the case when neoplasms invade muscular tissue. Lipoma of the *bones* is rare. We have seen one example of it in the body of the femur. The compact tissue of the bone was here transformed into a spongy tissue with thin trabeculæ and large aveoli filled with adipose tissue; the stroma of the tumour, instead of being formed as in lipoma generally of fibrous tissue, was composed of osseous trabeculæ. Lipoma of the *glands*, particularly that of the breast, may acquire a considerable size. In the *breast*, the adipose tissue of new formation is disposed around the galactophorous ducts and acini; the organ preserves its form, but acquires an enormous size and weight. When the cellulo-adipose tissue surrounding the *kidney* or *lymphatic glands* greatly hypertrophies a *capsular lipoma* is said to be formed; atrophy of the organ thus enveloped is not a necessary consequence.

Varieties of Lipoma.

1st. **Pure lipoma**, composed simply of pure cellulo-adipose tissue and a small quantity of connective tissue surrounding the lobules. The latter are large and well defined and distinctly give the characteristic sensation of false fluctuation.

2nd. **Myxomatous lipoma** is that in which mucous tissue is found between the adipose vesicles; it does not differ from lipomatous myxoma (see fig. 77).

3rd. **Fibrous lipoma** is that in which connective tissue is very abundant. This is the adipo-fibrous tumour of Cruveilhier, and the steatoma of the older writers. To diagnose this variety of tumour histological examination is necessary, as otherwise it might be confounded with pure fibroma or carcinoma.

4th. **Osseous lipoma** is represented by the solitary case we have given above, in which the tumour was traversed by osseous trabeculæ.

5th. **Erectile lipoma.** The blood-vessels are very numerous and distended, particularly when the tumour projects on a serous or mucous membrane.

The nutritive changes to be studied in lipoma are:—

a. Fatty degeneration which seems a mere pleonasm. The fat vesicles break down into fine granules, and in the place of large cells or vesicles filled with a single drop of oil, there are granular bodies. To the naked eye the tissue is then opaque, grey in colour and of a peculiar consistence, resembling that of a sarcoma or carcinoma undergoing fatty degeneration.

b. Pedunculated lipomata may become *necrosed* by their pedicle being ruptured and falling into a natural cavity. This occurs especially in the peritoneum where, by the hypertrophy of the appendices epiploicæ, they become in fact small, fatty polypi; on becoming detached and falling into the peritoneal cavity they break up, their fat is decomposed, fatty acids are set free and cholesterin separates, while the capsule which surrounds the little tumour grows in density and constitutes a cystic envelop.

c. Calcareous degeneration may take place and stony masses be produced.

d. Projecting and voluminous lipomata are often affected by *inflammation* and *ulceration.* Embryonic tissue is developed, the fat vesicles are partly absorbed, while the tumour becomes harder.

Development of lipoma.—The development of lipoma is little understood. Förster considered that lipoma was developed from a mass of embryonic tissue, the cells of which were afterwards infiltrated with fat. He adduced this opinion from the fact that islets of embryonic tissue are sometimes found in the centre of lipoma. Virchow thinks that the adipose tissue of lipoma proceeds from mucous tissue. There is, it is true, a close relationship between mucous and adipose tissue; mucous tissue represents in fact a stage in the development of connective tissue, and tumours in which mucous and adipose tissues are mixed in different proportions are not rare (mucous lipoma or lipomatous myxoma, see fig. 77). Förster explains the growth of lipoma by another theory; he mentions having seen the adipose cells elongate, become restricted at a point, and divide. This would be a true proliferation of fat vesicles. We think that there is here an error of interpretation. Adipose cells are indeed so easily deformed by pressure, that in preparations of them they may be observed elongated and bean-shaped, without their being necessarily in process of division. Although embryonic cells or mucous tissue cells mark the first step in the neoplasm, it is in these cells, which are but slightly differentiated from one another, that the fat is deposited. This is the ordinary mode of development and the one best understood.

Prognosis of lipoma.—Lipoma is serious only when from its volume it prevents the performance of some function, or when it gives rise to inflammatory accidents, for example, inflammation of a serous membrane.

The anatomical diagnosis is so easy even with the naked eye that there is no necessity to insist upon it.

Class IV. Carcinoma.

The class **Carcinoma** comprehends those tumours, which by their aspect and gravity seem removed from the other classes of tumours, the type of which is found in the connective tissues. They nevertheless belong to them by reason of their origin, their mode of development, their constitution, and particularly their stroma, the essential element in their definition.

Synonyms.—Carcinoma is also called *alveolar*, *scirrhous*, and *encephaloid cancer*. The word 'cancer' is vulgarly given to any malignant tumour which spreads rapidly and causes secondary growths; but though thus employed by most medical men the term has no histological signification and defines no tissue. The words encephaloid and scirrhous correspond to varieties of carcinoma and have a meaning based on gross appearances. A tumour which resembles softened cerebral substance is called encephaloid, while a hard tumour is scirrhous. Carcinoma was formerly considered by pathological anatomists to be characterised by a so-called cancer juice, discovered by Cruveilhier, but, as we have already shown, this juice may be obtained from sarcomata, which also often have the appearance of encephaloid and scirrhous tumours. The words 'scirrhous' and 'encephaloid' as understood by the old writers no longer describe a definite tissue.

Definition.—The word carcinoma, first employed in Germany in the same vague sense as cancer, has lately received a more precise definition based on histological study. It is, however, not yet sufficiently rigorously defined, since Förster, for example, speaks of 'carcinoma properly so called' and 'epithelial carcinoma,' the latter being cancroid or epithelioma, quite distinct from carcinoma, as we shall see further on. This confusion is due to the fact that the true characters of carcinoma and epithelioma have not been recognised. The latter has the structure and mode of development of epithelial tissue, while carcinoma belongs to the connective-tissue type. The word 'carcinoma' is not of more value than that of cancer, both having the common root *cancer*, crab, from a gross resemblance certain tumours, traversed by superficial veins, have with this animal. To be logical and to give each tumour the radicle of the tissue it approaches nearest, carcinoma should be called alveolar fibroma; nevertheless, not to change a name received and adopted by all, we will continue to employ the word carcinoma defining it in the following manner: *Carcinoma is a tumour composed of a fibrous stroma limiting alveoli, which by communicating with one another form a cavernous system; these alveoli are filled with free cells separated from each other only by a more or less abundant fluid.*

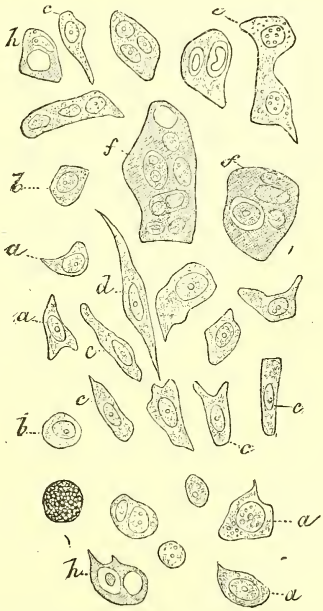

Fig. 88.—Cells from Carcinoma Juice.

a, tailed cells; *b*, round cells; *c*, prismatic cells; *d*, fusiform cells; *e*, an hour-glass-shaped cell; *f*, *h*, cells undergoing mucoid degeneration (the physaliphorous cells of Virchow).

General description of carcinoma.—The contents of the alveoli and the stroma are the parts to be studied. The contents of the alveoli form the milky juice of cancer. It is easily squeezed from the cavernous tissue in which it is contained by scraping or by pressure. When this juice is examined under the microscope, a large number of **carcinoma cells** of every conceivable variety of shape and size are observed. Some are round, small, and measure 9 μ or 10 μ, others also spherical, but larger, and may reach 20 μ, 40 μ, or even more; some are polygonal, with rounded or extremely sharp angles—such are the tailed or racket-shaped cells, one extremity being elongated while the other is enlarged. Nothing can be more varied and unexpected than the forms; some carcinoma cells appear flat when their surface is seen, and narrow viewed in profile, which may be well observed as they roll over and over under the eye of the observer; they may be elongated in a fusiform manner, like the cells of fasciculated sarcoma. A similar variety of form, though less pronounced, may be, as we have seen, met with in sarcoma. All the cells have one or many nuclei; there are sometimes as many as fifteen or twenty in one cell; they are spherical or oval, and contain one or many nucleoli, generally well developed. The nuclei are large and from 9 μ to 20 μ or 30 μ, the nucleoli themselves sometimes measuring 5 μ to 9 μ. When large they appear vesicular; the nuclei are surrounded by a double line as if they possessed an enveloping membrane. Similar forms of nuclei and nucleoli are met with in sarcoma, sometimes even in purely inflammatory neoplasms; they therefore, no more than the cells, can assist in defining carcinoma; neither can the polymorphous state of the cells be depended upon to characterise carcinoma, for in some tumours all the cells may be similar, either round or polygonal. Carcinoma cells are polygonal by reciprocal pressure when contained in a cavity where the intercellular substance is slight. The anatomical reason of this form of the cells is the same which determines the tesselated form of epithelial cells, and from this resemblance some authors have concluded a natural analogy, and the terms epithelial or epithelioid have been used to designate carcinoma cells. These cells seem to have no enveloping membrane and are not cemented together, which fact differentiates them sharply from epithelial cells. They are subject to various nutritive changes. Sometimes they swell and become spherical as if infiltrated with serum. Often the nucleolus enlarges so as to fill the nucleus; hypertrophy of the nucleolus may be so great as to make the nucleus vesicular—such are the physaliphorous cells of Virchow (*h*, fig. 88). Similar vesicles are produced, not by the dilatation of nucleus or nucleolus but in the midst of the protoplasm itself, by a mechanism similar to that described by Dujardin when little cavities are hollowed in sarcode by the action of water. In these sarcodic vesicles, better called vacuoles, free granules are often present. Carcinoma cells undergo other changes of nutrition which we shall consider when treating of the varieties of carcinoma.

The **stroma**, the second essential constituent part of carcinoma, may be studied in dissociated fragments of tumours, or in sections from fresh or hardened specimens. It is composed of fibrous trabeculæ united so as to form a continuous system, each fibrous trabecula representing one or more bundles of connective tissue, between which are scattered ordinary connective-tissue cells, or cells slightly differentiated from them (fig. 91). These cells are indistinct if examined in the fresh state, but if acetic acid be added, the nuclei become distinct, the fibres swell, and the trabeculæ become transparent and homogeneous. It is still an open question if carcinoma contain lymphatics; Schrœder van de Kolk has injected them, and Rindfleisch thinks they form perivascular sheaths similar to those of the nerve cells. We will return to this point. When a very delicate section of carcinoma is examined, the cells being still *in situ*, it may be thought that each alveolus is closed, but, if the section be a little thicker and the cells be removed by brushing them away with a camel's-hair brush, it is easily seen that the tissue is cavernous, the cavities communicating with one another. For example, two cavities may be seen communicating with a third situated beneath them (see fig. 89).

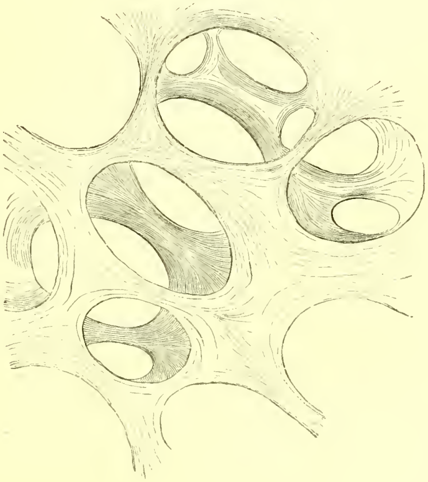

Fig. 89.

Stroma of carcinoma, from which the cells have been brushed away. Magnified 300 diameters.

Development of carcinoma.—The study of the development of carcinoma throws much light on its nature. To take first the development of carcinoma in bone, as an example, we observe that, at the beginning, the same phenomena occur as in inflammation. In the case of a short bone, the fat vesicles disappear and give place by proliferation to embryonic cells, the osseous trabeculæ are partially absorbed, and medullary spaces limited by festooned lamellæ are seen filled with embryonic medulla, as in rarefying ostitis (see fig. 185). This irritative process may end in a new formation of osseous tissue, when sclerosis of bone or condensing ostitis is produced. These phenomena of rarefying or condensing ostitis are the first phase, or the uncertain stage, in the development of primary carcinoma of the bone. Soon, however, the embryonic tissue is transformed into fibrous tissue, which is the second or fibrous phase. The cells contained in the fibrous trabeculæ give origin to a more or less considerable number of small cells, which are in close contact and packed together in a small space; by multiplying, these cells enlarge the spaces containing them and assist in the formation of the first alveoli of carcinoma. In the mamma, a similar development is observed. The trabeculæ of fibrous connective tissue, which enter into the structure of the gland and spread out thence into the neighbouring adipose tissue, thicken and become infiltrated with fluid. If a section be made after hardening and staining

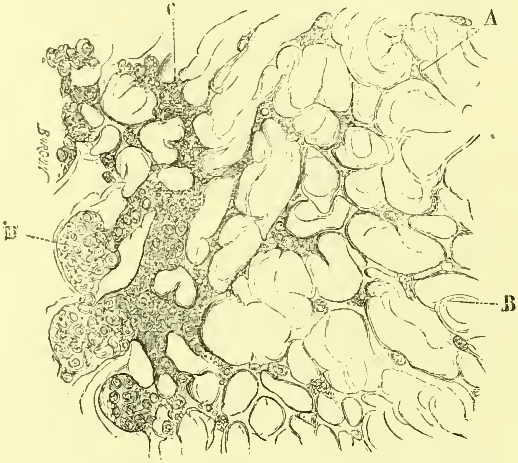

FIG. 90.—DEVELOPMENT OF CARCINOMA IN THE BREAST.

Section made after hardening in chromic acid. A. Plasmatic spaces which enlarge by the multiplication of their cells; at C they have preserved their angular form; at D they have become globular and form the alveoli of carcinoma. Magnified 150 diameters.

with carmine, it can be seen that the spaces included between the connective-tissue fibres contain globular cells isolated or united into groups, and that the formation of the alveoli of carcinoma is by the progressive growth of these groups of cells (see figs. 90 and 91) contained within the fibrous trabeculæ. These by their growth cause the absorption of the surrounding fibrous tissue which, on the other hand, becomes denser under the pressure exercised by the newly formed cells; this pressure exercised equally in every direction, is also probably the cause of the tendency the alveoli show to take the spherical form.

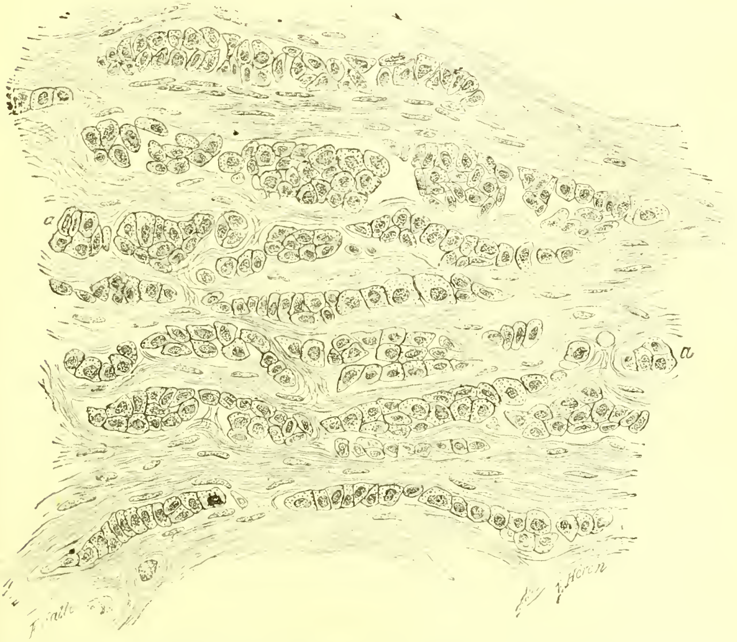

Fig. 91.—Development of Carcinoma in a Small Recent Nodule situated in a Fibrous Tract, near a Primary Tumour of the Breast.

s, bundles of fibrous tissue showing connective-tissue cells between them; *a*, carcinoma cells arranged in long lines or in alveoli between the fibrous bundles. Magnified 200 diameters.

In carcinoma of the mamma the cellulo-adipose tissue is preserved; the tumour increases, in fact, at the expense of the connective tissue of the trabeculæ which separate the lobules of adipose vesicles, the latter, however, remaining for a very long time intact in the midst of the morbid mass. The preservation of these adipose angular masses, seen on section of a tumour to be irregularly disseminated, has many times aided us in ascertaining with the naked eye the carcinomatous nature of a tumour; a diagnosis always verified by microscopical examination. The integrity of the adipose cells is explained by the fact, that in the breast, carcinoma develops chiefly in pre-existing fibrous tracts, and not from previously formed embryonic connective tissue. In the glandular tissue, in the acini and ducts, very interesting phenomena are at the same time taking place. The epithelium of the acini and ducts proliferates in consequence of the irritation in their neighbourhood; the acini become filled with cells and hypertrophy, so that it might be thought, there was a direct relation between proliferation of the epithelial cells and development of carcinoma; it has even been maintained that a carcinoma is a new gland destined to eliminate poisonous products from the organism, in the same way that the kidney eliminates urea. This view of the humoralists is, however, invalidated by the fact that removal of the tumour does not cause poisoning, but is on the contrary the only remedy. On the existence of new epithelial tissue in the acini and ducts of the mammary gland affected with carcinoma, is founded the idea of the analogy between the latter and a gland, an idea, which the development of the tumour as described above, is sufficient to destroy. In epithelioma, on the contrary, new epithelial tissue is never seen to be developed in isolated centres between adjoining bundles of connective tissue, but from masses of embryonic tissue, and in the form of buds springing from pre-existing epithelial tissue. Sympathetic irritation of the glandular acini and ducts gives rise nevertheless to rather important phenomena, to which attention is drawn. The epithelial cells of the galactophorous ducts multiply and fill up the lumen of the ducts, so that they appear like solid cylinders. On transverse section, the ducts are seen to be filled with epithelial cells cemented together and adherent to the walls, whilst the centre is occupied by round, opaque cells, undergoing fatty degeneration, free or united together so as to form a kind of plug, in which case the ducts are distended and filled with a grey or yellowish caseous mass. Their direction may be easily followed by a section of the breast passing through the nipple and the morbid mass. There is often during life an ichorous discharge from the nipple. At their further extremity the degenerated ducts terminate in irregular sinuous spaces corresponding to the destroyed acini, in the place of which there are often true cysts. These cysts are round or cavernous, sometimes large, and filled with a mucous or serous fluid, or with a detritus in which cellular elements, free fatty granules, and even blood pigment may be recognised. In all tumours of the breast, the galactophorous canals are the seat of changes and cysts similar to those described above; ichorous discharge from the nipple is, however, only observed in carcinoma.

The growth of carcinoma is at the expense of its own mass, or by invasion of neighbouring tissues. The proof that the tumour grows at the expense of its own tissue is, that in hardened sections spaces filled with cells are found in the trabeculæ of the fibrous stroma; these are in process of development into carcinomatous alveoli.

Growth by invasion of neighbouring tissues may be *continuous* or *discontinuous*, both modes being common in carcinoma. In continuous development the tracts of fibrous tissue which spread out from the breast into the adjacent parts undergo carcinomatous metamorphosis.

Secondary growths in organs far removed are preceded by induration and increase in the size of the glands communicating with the lymphatics of the tumour. How is it that carcinoma is the pathological tissue which most easily and almost invariably determines lesions of the lymphatic glands? It is because the alveoli of carcinoma are in direct communication with the lymphatic vessels. This communication may be easily demonstrated by injections. If with a Pravaz syringe, provided with a finely pointed canula, Prussian blue be injected into the alveoli of carcinoma, the injected fluid first fills the alveoli, marking out a more or less extensive cavernous system, and then penetrates into the lymphatic vessels issuing at the wound made in the operation. For the injection to be successful the tumour should be intact. Indurated glands in carcinoma do not always show, at the commencement, the structure of the primary tumour; sometimes they simply undergo fibrous change; but in the newly formed fibrous tissue alveoli are soon developed. These facts, which are often very marked, have nevertheless escaped the observation of writers preceding us; they, however, appear to us to be of great importance, for they lend support to our views as regards the morphological signification of carcinoma.

Varieties of carcinoma.—It is not possible to classify carcinoma according to the dimension or form of its cells, for they are often extremely variable even in the same tumour. Generally the softer the carcinoma the larger the cells, the harder it is the smaller they are. This is however not an absolute rule. The round or polygonal form of the cells is solely due to the larger or smaller quantity of intercellular substance present. We classify carcinoma according to the state of the stroma and the nutritive modifications of the cells.

I. **Fibrous or scirrhous carcinoma.**—When the trabeculæ are thick and resistant the carcinoma is called hard or scirrhous. In fine sections the fibrous trabeculæ appear attenuated, homogeneous and highly refractive; granular degeneration of the cells contained in the alveoli is often observed, or the cells may be destroyed and the resulting detritus is carried away by the lymphatics; the morbid tissue then shrinks, so that the alveoli, in which a little fluid and some fatty granules still remain, are almost effaced; the tumour is then called *atrophic scirrhus*. This atrophy does not take place in all parts of the tumour at the same time; it generally invades the centre. This part then yields no juice on section, but juice is obtained from the periphery where alveoli filled with cells are still to be seen. In the parts most profoundly atrophied, and where more or less ulceration is also frequently present, the shrunken stroma sometimes contains a great number of large elastic fibres in masses or arranged in parallel lines, or tangled together in a most irregular and intricate manner. Infiltration of the glands is soon observed in scirrhous cancer, but secondary growths are formed but slowly in most of the organs and tissues, while the primary tumour

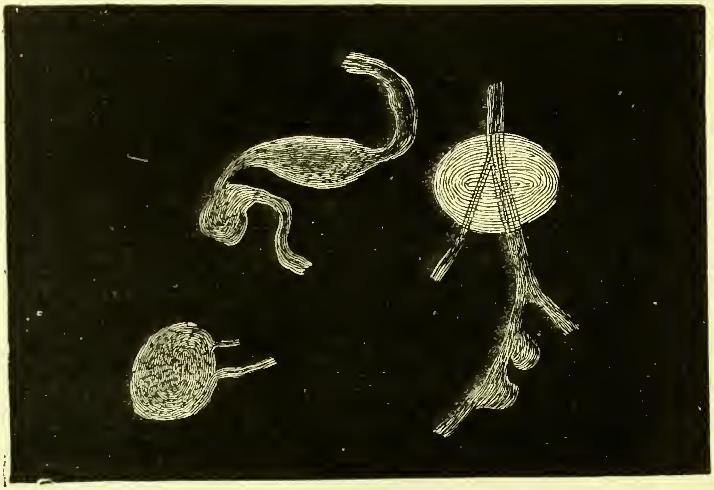

FIG. 92.—ANEURISMAL DILATATIONS OF CAPILLARY VESSELS IN ENCEPHALOID CARCINOMA.

Magnified 50 diameters.

increases slowly, or may remain stationary, or indeed almost entirely disappear.

II. **Encephaloid or medullary carcinoma.**—The trabeculæ are more delicate and the alveoli larger in this species than in the preceding; they may even be so large as to be visible to the naked eye. The stroma is weak and interstitial hæmorrhages are frequent, so that in section the tissue is variously tinted, white, grey, rose-coloured, red, yellowish and even brown, owing to the changes of the extravasated blood. The primary tumour grows much more rapidly than scirrhus, but secondary growths are generally less extensive.

Two varieties of encephaloid carcinoma may be distinguished:—

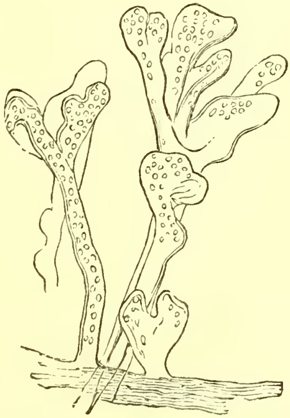

FIG. 93.—BLOOD-VESSELS BUDDING ON THE WALLS OF AN ALVEOLUS.

Magnified 150 diameters.

The *pultaceous form* in which the tissue is extremely soft, and out of the alveoli, which are very large, may be pressed a thick and abundant juice.

Erectile or hæmatode carcinoma.—In this variety, often associated with the preceding, the blood-vessels, which are numerous and well developed, present moniliform dilatations (see fig. 92) as well as little aneurismal tumours, visible to the naked eye as minute red points. The blood-vessels project into the interior of the alveoli and bud on their walls (see fig. 93); they often rupture and cause extravasations of blood.

The softness of encephaloid carcinoma may be solely due to the fact that the alveoli though small, are separated by divisions of extreme delicacy.

The following three species of carcinoma are produced by nutritive changes in their cellular elements.

III. **Lipomatous carcinoma.**—The cells in the alveoli may become filled with fat droplets and resemble adipose vesicles ; but they are not grouped together by bands of connective tissue, nor by capillary blood-vessels like the adipose globules of subcutaneous cellular tissue. We have twice observed this form of carcinoma, notably in the bones. It so closely resembles lipoma that it may, at first sight, be confounded with it, if all the elements of the problem be not considered. The cells are not destroyed by the adipose infiltration. We have seen one example of generalisation of lipomatous carcinoma, in which all the secondary growths presented the same characters; this fact justifies our describing it as a distinct species.

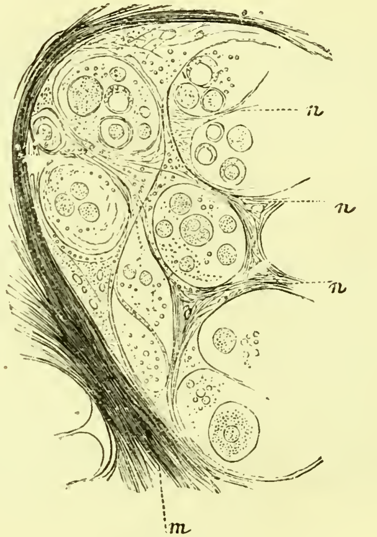

FIG. 94.—COLLOID CARCINOMA.

m, thick fibrous trabeculæ ; *n*, thinner trabeculæ containing cells in a state of mucoid degeneration, and limiting alveoli filled with cells, which have also undergone mucoid degeneration. Magnified 300 diameters.

IV. **Mucoid or colloid carcinona.**—Colloid degeneration of carcinoma cells gives them a characteristic, gelatiniform appearance, which is reproduced in the secondary growths. Thus it is a distinct species. The alveoli of colloid carcinoma do not differ from every other form of carcinoma ; the trabeculæ are only easier to see being filled with a mucoid fluid. The cells, infiltrated with droplets of mucin, become spherical and vesicular, and are finally destroyed, Those which persist sometimes attain an enormous size; but there are only a few in each alveolus suspended in a fluid equally mucoid. The alveoli distended by the fluid become regularly spherical. As is always the case in mucoid degeneration, there is also some fatty degeneration of the cells. The stroma of the tumour may be unmodified, sometimes the trabeculæ are œdematous and the fibrils separated by a fluid substance, or they may also undergo mucoid degeneration and become much thinner or be destroyed. The morbid mass may then contain portions, more or less extensive, in which colloid change is so marked that they seem simply formed of an amorphous substance containing scattered groups of cells. To the naked eye these groups of cells appear as so many small opaque spots. Generally some connective-tissue fibres, arcs of circles limiting spaces, remnants of the old trabeculæ, remain around these groups of cells (fig. 94). The tumour is not homogeneous, and the alveoli, which have undergone such advanced colloid degeneration, form groups separated from others by ordinary fibrous tissue. It is this arrangement which to the naked eye gives the tumour an alveolar appearance. The blood-vessels of colloid carcinoma are often dilated, and sometimes rupture and cause extravasations of blood.

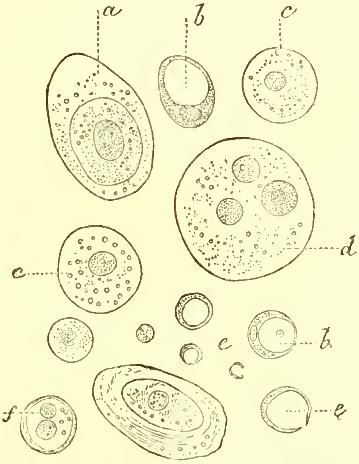

FIG. 95.—CELLS OF COLLOID CARCINOMA.

a, large cell enclosing another cell; *d*, mother-cell; *c*, cells infiltrated with colloid material; *b*, cell filled with a colloid drop; *e*, cells reduced to a film undergoing destruction. Magnified 350 diameters.

V. **Melanotic carcinoma.**—Melanotic carcinoma is rarer than melanotic sarcoma. In this species the cells in the alveoli show melanotic granules in their interior. The trabeculæ may also become infiltrated with the same granules, which are then deposited in the connective-tissue cells proper to the trabeculæ.

Independently of the preceding species, each of which possesses the property of producing secondary growths having its specific characters, the following changes may be observed in every carcinomatous tumour:—

a. **Fatty degeneration.**—In every old carcinoma, parts varying in extent, those at the centre in particular, present traces of fatty degeneration. In an alveolus, for example, some cells are found filled with fine, fatty granules, looking with a low power like opaque blocks, and not differing from granular bodies except by their larger size due to the dimensions of the carcinoma cells. When fatty degeneration is very marked, the parts affected are yellow and more or less opaque. The capillary walls and the protoplasm of the connective-tissue cells of the stroma may also be affected with the same degeneration. The intra-alveolar cells being destroyed and the degenerated trabeculæ broken down into a detritus which is taken up by the lymphatics, a shrinking or partial atrophy of the tumour results. In secondary deposits in the serous membrane or liver, this atrophy is characterised by a falling in of the centre which originally projected. In the skin, and particularly in the mammary gland, atrophy is shown by a depression in the form of a hard or callous cicatrix.

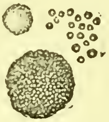

Fig. 96.—Granular Bodies and Free Fatty Granules observed in Carcinoma, also in Cerebral Softening and in Fatty Degeneration generally.

Magnified 300 diameters.

b. **Caseous degeneration.**—In all rapidly growing tumours, carcinoma in particular, obliteration of the vessels may occur, caused either by fibrin, or by excrescences or buds forming on the veins. These buds, generally supplied with blood-vessels and composed of carcinomatous tissue, may be developed at a distance from the primary tumour; they thus form true cancerous emboli. They are more often observed in the portal vein, and in the iliac and axillary veins, when the latter traverse the centre of a primary tumour, or are surrounded by degenerate lymphatic glands. The parts of the morbid mass deprived of the circulation of the blood are slowly destroyed, ulceration resulting if the tumour projects upon a cutaneous or mucous surface, or infarcts if seated within a viscus. These infarcts undergo caseous melting; the softened parts are taken up by the circulation, and a depression is produced. Infarction is recognised when the small vessels are found filled with a granular mass. Whether consequent on initial fatty degeneration, or on arrest of the circulation, whether slow or rapid, this atrophy characterises a distinct clinical variety, atrophic scirrhus, scirrhus in cuirass, the fibrous carcinoma of Billroth. If fine sections be examined, parts of the tumour seem formed of a fibrous tissue, in the meshes of which only a few fatty granules are found ; the alveoli, the cells of which have been destroyed, are collapsed, in proof of which they may be compared with other parts, where the carcinomatous tissue is in a less senile condition.

Calcareous transformation is rare in carcinoma. Near to bones, however, the stroma may sometimes undergo this change, producing what has been incorrectly called ossifying carcinoma. (Paulicki).

c. **Inflammation of carcinoma.**—Carcinoma may become inflamed and ulcerated, either as the result of traumatism or by progress of the tumour. What occurs is very interesting and aids, together with development, in explaining the true nature of carcinoma. An active proliferation of the cellular elements contained within the alveoli is observed near the ulcerating point, the cells divide and give origin to elements having all the characters of embryonic cells ; they measure 8 μ to 10 μ, but the granular and refractive protoplasm of which they are composed mask their nuclei. The alveoli break down and are lost in a mass of embryonic tissue, in the midst of which are still found a few fibrous trabeculæ of the stroma. The embryonic tissue, which constitutes the base of the ulcer, takes on the surface the form of highly vascular granulations. The newly formed vessels, the walls of which are composed of young cells, resemble those of granulation tissue. Thus the cells contained in the alveoli take the embryonic form as a consequence of the irritative influence of inflammation. A similar change is never observed in the cells of epithelioma.

d. **Villous carcinoma.**—Whatever may be the variety of carcinoma, if it attacks a cutaneous or mucous surface, granulations spring up on the surface immediately after ulceration. These villous granulations are sometimes much longer than simple granulations, and are also numerous and pressed together. It is these which give the tumour the name of villous carcinoma. The blood-vessels, not being sustained by a solid framework, present small aneurismal dilatations, and are often the point of departure of repeated and considerable hæmorrhages.

Anatomical diagnosis of carcinoma.—The anatomical diagnosis of carcinoma is very difficult to make with the naked eye. Pathologists have indeed in the past confounded carcinoma with every malignant tumour, and even with infarcts, till recourse was had to microscopical examination. The presence of the so-called cancer juice is not sufficient. We have seen that a similar fluid may be obtained from sarcoma a short time after removal, and always from tumours on the cadaver twenty-four hours after death; we shall find that a similar fluid can be obtained from soft epithelioma and from lymphadenoma whatever may be its seat; the same with infarcts and tissues affected with diffuse suppuration. The cells of carcinoma have in themselves nothing characteristic; to be certain of the presence of carcinoma it is necessary to recognise the alveolar nature of the stroma and the form of the contained cells. Sections, delicate enough to submit to microscopical examination, can be made in the fresh state, if care be taken to moisten the surface well and not to press hard with the razor; no error is possible if the preparation be previously hardened in a ·2 or ·4 per cent. solution of chromic acid, or in alcohol, picric acid, or in gum and alcohol. The peculiar cavernous arrangement of the stroma of carcinoma always differentiates it from sarcoma, in which fibrous trabeculæ parallel to the vessels may be met with, but never regular alveoli. Colloid carcinoma, which with the naked eye may be confounded with myxoma, differs from it by its alveolar stroma; in myxoma not only is there no stroma, but a perfectly characteristic network of anastomosing connective-tissue cells may be observed. Atrophic carcinoma may be confounded with fibroma, if the collapsed alveoli of the atrophied parts are only examined; but the unmistakable characters of the periphery of the tumour will remove all hesitation. On the other hand, in fibroma there are never free cells comparable to those contained in the alveoli of carcinoma. The anatomical diagnosis of carcinoma and epithelioma will be made when treating of the latter.

Prognosis of carcinoma.—Whatever may be the seat, the species, or the variety of carcinoma it is always fatal; but the duration of the disease and consequently its gravity varies according to the species. The encephaloid form is that in which the primary tumour most rapidly acquires a great size by invading neighbouring tissues; the scirrhous, particularly the atrophic variety, is remarkable for the slight tendency the primary tumour has to extend, and for the slowness of its growth. In infirmaries this form of tumour may be seen dating ten or fifteen years back; but nevertheless it always terminates by the production of secondary growths extending to the greater number of organs the longer the disease has been established. It is difficult to decide if generalisation is due to the particular species of tumour or to its long duration; indeed, encephaloid carcinoma may become very rapidly generalised. We must draw attention to the fact that the development and generalisation to many organs of little secondary nodes of scirrhus does not always cause death rapidly, though such is constantly the end.

Carcinoma is developed primarily in all the organs, but viscera lined by mucous membrane and glands, especially the stomach, uterus, and breast, are more frequently attacked by it. The primary tumour constantly infects the corresponding lymphatic glands.

We have now completed the description of those tumours composed of connective tissue which are characterised by hypertrophic aberration of the cellular elements, and we shall now proceed to study those tumours in which, on the contrary, the cells atrophy; of such are syphilitic gummata, tubercle, and glanders. These three species of tumours have this in common, that they are each in relation with a general constitutional disease.

Class V. Syphilitic Gummata.

From the anatomical point of view the most characteristic lesions of syphilis are gummata; but every syphilitic neoplasm is not a gumma, and in many of these neoplasms no anatomical difference can be found between them and those caused by simple inflammation. We will rapidly pass in review the various syphilitic accidents, for studied alone, gummata would not be sufficiently understood, and it is desirable moreover to indicate their place in the history of syphilis.

The lesions determined in connective tissue by *hard chancre*, or the primary accident of syphilis, do not differ essentially from those produced by inflammation in the same tissue. At the base of indurated chancre, cells are met with resembling those of granulation tissue, they are round or fusiform embryonic cells, and are situated in the midst of an amorphous or fibrillar, and resistant ground substance, to which the chancre owes its induration. If characters distinguishing indurated chancre from simple inflammation are ever found, they will be discovered, we think, in this ground substance. The blood-vessels contained in the indurated tissue of chancre are well preserved, but their walls are extremely thick and the lumen very narrow. This thickening is the result of an inflammatory process causing lesions absolutely similar to those of chronic arteritis. Bærensprung thought that the indurated tissue at the base of chancre was impregnated with an amyloid substance, capable of being coloured blue-violet by iodine and sulphuric acid; this opinion, however, has not been verified by other observers, and we have tried in vain to obtain the reaction indicated by him. When indurated chancre heals, the newly formed embryonic tissue tends to develop into adult connective tissue. (For fuller details see the article 'Skin.')

All the neoplasms of constitutional syphilis, both primary and secondary, tend on recovery to reproduce the previously existing tissue. Thus a papulo-squamous syphilide leaves no trace at the end of a certain period; the same with lesions, of the same period, of deeper parts, of the periosteum, bones and parenchymatous organs. Affections of the bones and liver may be cured without leaving traces, or only a simple or hypertrophied cicatrix such as a hyperostosis.

Syphilis is usually divided into *primary*, *secondary* and *tertiary periods*, the term *secondary* being applied particularly to superficial mucous or cutaneous syphilides, the word *tertiary* to lesions of the bones and parenchymatous organs. This division does not seem to us to be accurate. It would be truer, from the pathological point of view, as Virchow has indicated, if the purely inflammatory lesions of syphilis were called secondary, and the later lesions, which manifest themselves under the form of tumours, were called tertiary.

To thoroughly comprehend the phenomena of syphilis the lesions should be studied separately in each tissue and in each organ. In the *bones*, contemporary with secondary accidents, pains, called rheumatoid by Ricord, but which are not due to permanent lesions, are observed; later, chronic inflammation shows itself on the surface of the bone, or under the periosteum (periostitis or periostoses), or is more profoundly seated causing ostitis, which is, at first, of the rarefying variety with thinning and destruction of the bony lamellæ, ending later in the production and condensation of bone tissue. This condensation, by obliterating the Haversian canals, may cause necrosis. At a later period true gummata may form. Thus in the bones, syphilis may give rise to ostitis, hyperostoses, necrosis and gummata. In the *liver*, there is at first interstitial hepatitis either diffuse, generalised, or circumscribed, but always characterised by fibrous tissue of new formation ; later, veritable gummata appear. In the *testicle*, there are also fibrous neoplasms, interstitial at first, then gummata. In the *lung*, there is also interstitial pneumonia, which may be diffuse or limited. The lesions of circumscribed pneumonia have often been regarded as gummata of the lung ; Virchow described them under the name of white hepatisation. They are observed in new-born infants and in very young children, in the form of nodules, the seat, extent, and number of which are very variable. Their structure is analogous to that of fœtal lung. In this, as is well known, the alveoli are separated from one another by an embryonic connective tissue rich in cells ; in syphilitic pneumonia, the inter-lobular

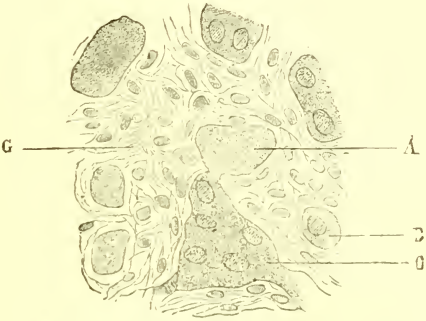

FIG. 97.—DIFFUSE SYPHILITIC INTERSTITIAL HEPATITIS.

A, C, liver cells undergoing fatty degeneration ; B, isolated hepatic cell ; G, new connective tissue. Magnified 300 diameters.

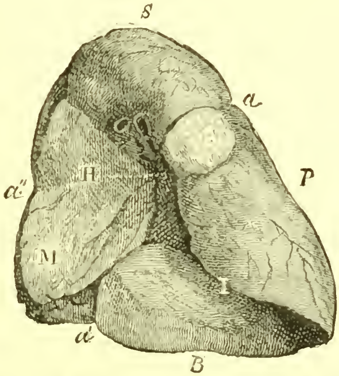

FIG. 98.—LUNG OF A NEW BORN INFANT (REDUCED ONE THIRD).

S, apex ; B, base ; H, hilus ; *a*, nucleus of syphilitic interstitial pneumonia.

connective tissue is thick and contains a large number of embryonic cells, while the narrowed alveoli are lined and even filled with epithelial cells, which are of the pavement form where in contact with the walls, but round in the centre of the alveolus. These cells soon undergo fatty degeneration; to the naked eye the alveoli then appear like small opaque spots; the degenerated cells are finally destroyed and absorbed, and the embryonic tissue becomes rapidly organised into fibrous tissue, and forms a small, hard tumour, in the midst of which true gummata may develop. Besides this special form of pneumonia, nuclei of variable size of catarrhal pneumonia may be observed in syphilitic children, which nuclei subsequently undergo caseous degeneration; most observers refer this lesion to syphilis. Syphilitic neoplasms, such as we have mentioned in the liver, testicle and lung, may show themselves in the *skin* and other organs. They resemble ordinary fibromata, there are no elastic fibres, and the connective-tissue fibres intersect in every direction. The cells often undergo fatty degeneration, and are then recognised under the microscope, with a low power and transmitted light, as blackish islets. At the centre, these fibromata often undergo mucoid degeneration. Though clinically considered as true gummata, they have not altogether their histological characters, and may be looked upon as intermediate between inflammatory neoplasms and gummata.

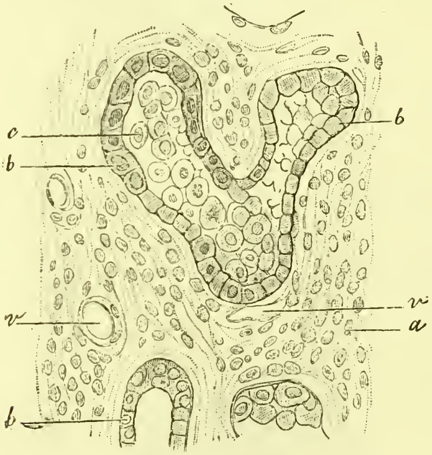

Fig. 99.—Transverse Section of the Nucleus of Hepatisation represented at *a* in the preceding Figure.

a, connective tissue of the lung proliferating; *b*, pavement cells arranged around the alveolus; *c*, free spherical cells within the alveolus; *v*, vessels. Magnified 300 diameters.

Authors are not agreed as to the place syphilitic gummata should occupy among tumours. Ricord, adopting John Hunter's views, regarded them as the result of the effusion of plastic lymph. When the microscope was first applied to the study of pathological anatomy, Lebert tried to find a specific element in gummata, but to his own regret was unsuccessful. Ch. Robin published his views in the thesis of Van Oordt. He holds that gummata are characterised by 80 per cent. of cyto-blastions, which are, according to him, small cells or free nuclei, measuring 5 μ to 6 μ, and are uninfluenced by acetic acid. In our opinion these elements are nothing else than embryonic cells hindered in the process of development by being too numerous and pressed together, or embryonic cells in a state of atrophy. Förster places gummata among tumours composed of lymph cells, for he compares the cellular elements of gummata to the cells contained in the follicles of the lymphatic glands. If the reticulated tissue peculiar to lymphatic glands were developed in gummata we could understand the analogy; but we cannot admit a similarity based on a comparison between the cells of gummata and those of the lymphatic glands, there being nothing characteristic in the latter. Virchow thinks that gummata are composed of granulation tissue. Lancereaux says that they are produced by proliferation of the connective tissue and does not define them in any other way; this definition is insufficient, for it applies to all tumours developed from connective tissue. According to Billroth, gummata are formed of a tissue purely and simply inflammatory; they are however tumours by their volume, form, and duration. Ernest Wagner has tried to define gummata according to their histological structure; he considers them to be formed of a peculiar tissue composed of small cells, enclosed in an isolated manner in cavities limited by a ground substance, and has given them the name of syphilomata.

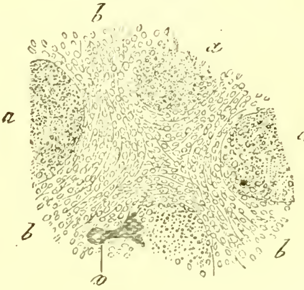

FIG. 100.—SYPHILITIC GUMMA OF THE LIVER.

a, centres of nodes in which the cells have become granular; *b*, periphery of the nodes; *v*, vessel. Magnified 100 diameters.

Description of gummata.—Gummata are tumours of variable size, so blended with the neighbouring tissues that they have no distinct limits and therefore cannot be enucleated. They form elevations on the surface of the organs in which they are developed. Seen in section with the naked eye, they appear to be composed of a greyish rose-coloured tissue, more or less vascular, and they have no juice. This absence of juice, joined to the firmness of the tissue, differentiates them at once from granulation tissue. By scraping, small fragments may be removed, on examining which cells varying in form may be found; these are (*a*) round embryonic cells 10 μ to 15 μ in diameter, the nucleus of which is made visible if acted upon by water and acetic acid; (*b*) fusiform or irregularly shaped cells; (*c*) small atrophied cells, measuring 5 μ to 6 μ, almost entirely filled with a nucleus, and placed side by side in a granular ground substance. As is obvious, these elements obtained by scraping, are not sufficient to afford the basis of a definition of gummata, unless the characters of the tissue and the process of development be also taken into consideration.

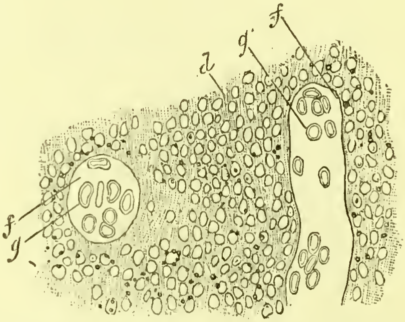

FIG. 101.—THE SAME PREPARATION AS THAT REPRESENTED AT FIG. 100, BUT MAGNIFIED 400 DIAMETERS.

d, elements of the gumma; *f*, blood-vessels in which red corpuscles, *g*, are seen.

If a thin section of a gumma, in process of evolution, be examined under the microscope a series of nodules are observed, each possessing its own centre of development. These nodules, more or less defined by their form and borders, are remarkable from the fact that in the centre of each the cells are small and have broken down into a molecular detritus, while the cells at the periphery are voluminous, round or fusiform and are blended with those of the neighbouring tissues (fig. 100). The blood-vessels penetrate the periphery of each nodule and may ramify in the centre; they are permeable to blood even when the nodules are in a state of atrophic degeneration; this fact makes a distinction between gumma and tubercle. Gummata remain vascular during the whole time of development, and the fibrous or embryonic tissue intermediate between the nodules is equally rich in blood-vessels. The nodules composing a gumma are very irregular as regards form and size; they measure on an average from $\frac{1}{15}$ to $\frac{1}{10}$ mm. in diameter. Gummata in process of evolution are rarely seen in the adult in post-mortem examinations, but they are frequently met with in the liver of new-born infants.

The development of gummata is very interesting. It may be divided into two phases: in the first phase there is simply proliferation of connective or an analogous tissue, the medulla of bone for example. In the *liver*, multiplication of the elements of the interstitial connective tissue is first observed; but this interstitial hepatitis differs greatly from that of ordinary cirrhosis, the result of alcoholic excess. Normally, the lobules of the liver are almost in contact, separated only by a thin layer of connective tissue which gives support to the extralobular vessels and bile ducts; from the periphery of the lobules the capillaries of the portal vein ramify toward the central intralobular vein. In simple atrophic cirrhosis, there is proliferation of the interlobular connective tissue, so that the hepatic lobules are separated from one another by broad zones of new connective tissue, in consequence of which the lobules atrophy (fig. 102). In interstitial syphilitic hepatitis,

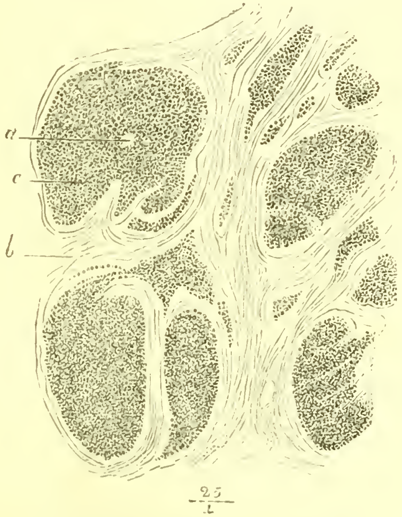

FIG. 102.—ALCOHOLIC CIRRHOSIS.

b, thickened interlobular connective tissue; *c*, hepatic lobule; *a*, central vein of the lobule. Magnified 25 diameters.

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the proliferation of connective-tissue cells does not take place between the lobules, but within them, along the course of the capillaries up to the intralobular vein. The result is that the trabeculæ of hepatic cells are everywhere surrounded by a new formation of connective-tissue cells arranged in rows (see fig. 97). This lesion may be observed in the adult, the new-born infant, and the fœtus dead before birth. In the liver, gummata are always preceded by this formation of embryonic tissue, which takes place sometimes throughout the whole organ, sometimes in limited spots. Later on, in the second phase of the development of gummata, the embryonic cells multiply, diminish in size, are pressed together and little nodules or irregular lobules are produced, in the centre of which the cells are atrophied and granular, while those at the periphery are large and resemble embryonic cells. The fundamental substance is slightly fibrillar and resembles connective tissue. Most descriptions of gummata apply only to very old foci; those given by Lancereaux, for example, are of gummata in a state of degeneration and not of evolution.

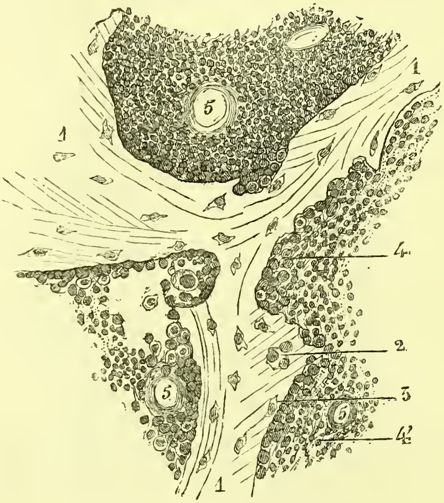

FIG. 103.—SYPHILITIC OSTITIS.

1. Osseous trabeculæ with notched borders in which are seen uni-nucleated bone corpuscles at 3, and multi-nucleated at 2. 4. Medullary tissue. 4′. Atrophied elements of this tissue. 5. Vessels which are permeable. At the upper part of the figure the cells are atrophied and undergoing caseous change.

In *bone* also, a gumma is preceded by proliferation of the cells of the medulla, in consequence of which the Haversian canals and the alveoli of the spongy tissue are filled with embryonic tissue, as in ostitis; the osseous trabeculæ are absorbed and gummatous nodules develop in the enlarged medullary spaces which are filled with embryonic tissue.

In the *skin* and subcutaneous cellular tissue, gummata develop as in the liver. Infiltration of the corium and subcutaneous connective tissue with a large number of small round cells first occurs, and it is only later that true gummatous nodules are formed. By reason of their situation gummata of the skin inflame, suppurate, and cause crateriform abscesses, which have a tendency to become chronic (for fuller details see Histology of the Skin).

The **structure of gummata** is as variable as their evolution.

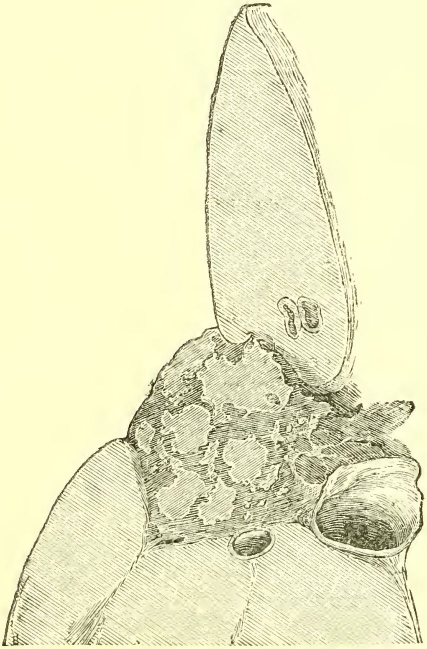

FIG. 104.—GUMMA OF THE LIVER.

In some cases they are formed almost entirely of fibrous tissue, which at a given moment in their evolution, undergoes mucoid or colloid degeneration. When, owing to inflammation, the surface is broken, there is a discharge of a mucous or gummy fluid (hence the origin of the name gumma), soon superseded by true pus. Mucoid degeneration is never seen except in what are clinically called gummata of the skin; but a peculiar caseous degeneration, giving to gummata their consistence and hardness, is not unfrequent. This consistence suffices to differentiate gummata, which are always hard even when caseous, from infarcts and tubercles which soften when in a state of caseous degeneration.

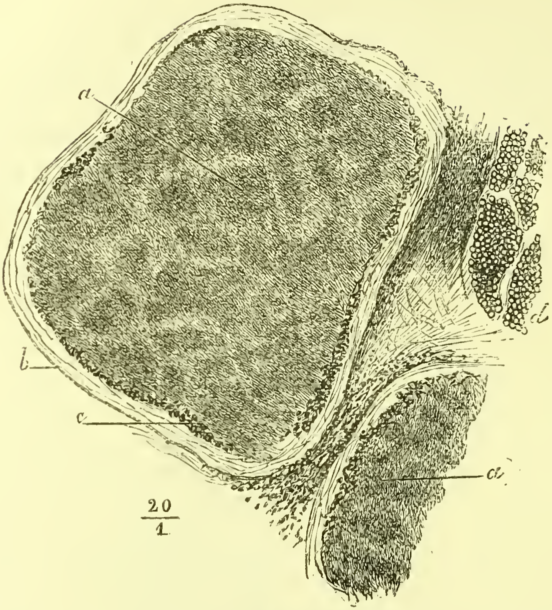

Fig. 105.—Section of Old Gummata of the Liver, cut after hardening in Chromic Acid.

a, angular masses surrounded by fibrous tissue, *b*; *c*, dark zone in which spaces are observed filled with fatty granules. (This zone is shown magnified with a higher power in fig. 107.) *d*, hepatic lobule. Magnified 20 diameters.

Long existing gummata of the liver in the adult show rather peculiar appearances. In the substance of the liver, which elsewhere may have preserved its physiological aspect, angular masses

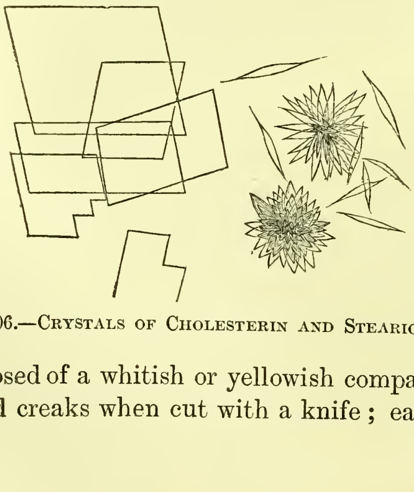

Fig. 106.—Crystals of Cholesterin and Stearic Acid.

are found composed of a whitish or yellowish compact tissue, which is very hard and creaks when cut with a knife; each one of these masses is surrounded by a fibrous zone, or they are all contained in one common fibrous mass. A more or less extensive and deep cicatricial depression is generally to be seen on the surface of the liver. These masses may be met with in the superficial or deep parts of the liver, and they may be so extensive as to cause division of the liver. The yellowish-white lardaceous tissue composing them shows gummatous nodules, if studied in fine sections from fresh or hardened specimens. The centre of these nodules is occupied by fine, fatty granules, immersed in a fibrillar proteid substance, which becomes transparent when acted upon by acetic acid. At the same spots, round bodies are also found, dark by transmitted light, and which, at first sight, might be mistaken for Gluge's corpuscles, but they are really rhomboidal crystals in the form of needles regularly arranged round a common centre (fig. 106); they are in fact crystals of stearic acid resulting from the decomposition of fatty matters. In the fibrous zone surrounding the caseous parts, stellate or fusiform groups of regularly arranged fatty granules are met with. At first sight it might be thought that they corresponded to connective-tissue cells, but on studying them more closely, it is seen that many belong to large, long, and often broad spaces, and that they represent lymphatic lacunæ or canals (*b*, *c*, fig. 107); we are also of opinion that these lymphatic spaces and canals carry away

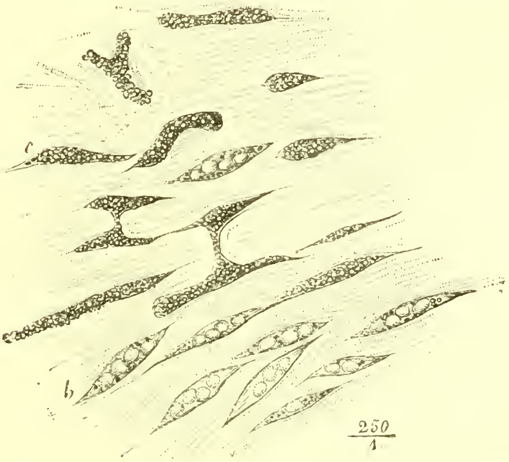

FIG. 107.—FIBROUS TISSUE FORMING THE ENVELOPE OF A GUMMA UNDERGOING DEGENERATION.

b, spaces enclosing cells and fatty granules ; *c*, the spaces containing only fat. Magnified 250 diameters.

the fat resulting from the degeneration of the lardaceous masses; indeed, the latter are destitute of vessels, while the fibrous tissue is vascular. The fibrous tissue seems then to play an important part, for the blood and lymphatic vessels which it contains absorb the products of decomposition of the gummatous nodules, when, yielding either to treatment or the natural progress of the disease, the gummata diminish and even completely disappear. When old gummata and the lardaceous masses constituting them have almost entirely disappeared, the fibrous capsule shrinks, but still remains closely united to the reduced caseous mass. Fibres may be seen issuing from it and penetrating the caseous mass, in which position they are seen to be surrounded by fine granules, and between them are small, round, granular cells which do not stain with carmine.

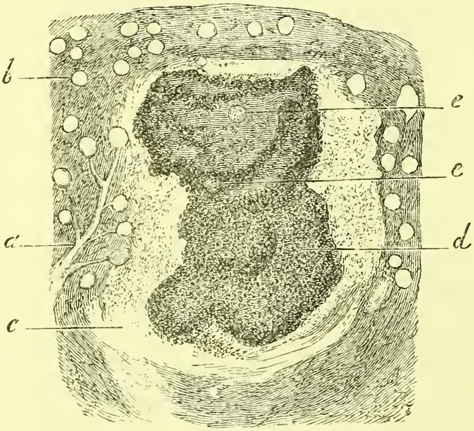

Fig. 108.—Old Gumma of the Kidney.

a, artery and glomeruli of the kidney; in the centre of the gumma the glomeruli, *e*, may still be recognised; *d*, opaque zone in which there are fatty granules; *c*, peripheral fibrous tissue. Magnified 20 diameters.

A few words should now be added on the histological process of the obliteration of blood-vessels in gummata undergoing caseous degeneration. As we have already said, it has been observed, notably in gummata of the bones, that caseous degeneration precedes vascular obliteration; hence it is not the consequence of it. The obliteration is caused, as in tubercle, by coagulation of blood in the vessels, which is preceded by inflammation of the vascular walls and proliferation of the endothelial cells. At the same time leucocytes collect and adhere to the internal wall of the vessel, so that an appearance is often produced simulating that of giant cells. True giant cells may be observed in the neighbourhood of syphilitic gummata, though they are rarer here than in tubercle.

Seat of gummata.—After the skin and subcutaneous cellular tissue, the organs which are most frequently the seat of gummata are, in the first place, the liver and the bones, then the testicles and kidneys. The reports hitherto published of gummata of the lung in the adult are not very conclusive, and the cases given as examples of pulmonary syphilis are not convincing; the lesions do not seem to us to present anatomical characters distinguishing them from tubercle. Moreover gummata must not be confounded with interstitial pneumonia described above (p. 190).

The anatomical diagnosis of true gummata is easy. It cannot be confounded with fibroma (composed of true fibrous tissue), for it presents little centres of proliferation which end in atrophy and a peculiar form of caseous degeneration. Its differential diagnosis from tubercle will be considered when studying the latter.

The prognosis of gummata is grave, not because they cause death by generalisation, nor by their number, which is generally small, but because they destroy the tissue in which they are developed, and convert it finally into cicatricial tissue. In the liver, when accompanied by interstitial hepatitis, they may cause all the symptoms of cirrhosis; in the bones, necroses, indelible cicatrices and loss of substance are the consequences; for example, perforations of the palatine arch and the bones of the skull. It is thus easily understood how gummata may disturb or destroy the function of the organs in which they are developed. But their gravity differs from that of carcinoma or sarcoma, inasmuch as they do not give rise to secondary growths. They are produced from one sole cause. They may be arrested in their course or even disappear under treatment by iodide of potassium.

Class VI. Tubercle.

The question of tuberculosis is overshadowed by contradictory opinions and is still obscure, but light begins to dawn upon it. Formerly every caseous mass was called a tubercle. The early histological researches of tubercle were not happy; Lebert thought he had found an element of characteristic form in the caseous masses he took as the type of tuberculosis; he had already described the famous 'cancer cell,' the 'tubercle corpuscle,' was its homologue; he had also searched, but without success, for the supposed characteristic element of syphilis. For some years all French histologists believed in the reality of Lebert's discovery. The tubercle corpuscles of Lebert are small, irregular, angular cells, 6 μ to 12 μ; on the addition of acetic acid they swell slightly while preserving their angular form, and a few fat granules become apparent, but no nucleus. These corpuscles are nothing else than dried, often fragmentary cells which have lost all vitality. Reinhardt and Virchow, the former whilst studying caseous pneumonia, the second in investigating lesions caused by infarcts, totally destroyed the theory of the specific element of tubercle. By experimentally inducing arterial emboli, Virchow produced fibrinous coagulation in the whole of the obliterated artery, and mortification of the cellular elements in the part deprived of nutritive fluid, and it was observed that these cells were transformed by dessication and granular degeneration into the so-called tubercle corpuscles. Similar lesions were soon found in carcinoma and sarcoma.

Virchow has attempted to prove that the characteristic of tuberculosis lies in the grey, semi-transparent granulation, an opinion generally admitted. Villemin made experiments to elucidate the nature of tubercle and to determine its place in pathology. He produced tubercular granulations in the rabbit and guinea-pig by inoculating them with the products of human tubercle; and he assimilates tuberculosis to virulent affections, such as glanders and syphilis. We ought nevertheless to add that other observers, Eberth, Wilson Fox, Sanderson, Cohnheim, &c., have determined products, analogous to tubercle, by inoculating animals with various pathological products. Cohnheim, who repeated these experiments, even maintains that it is sufficient to wound a rabbit to render it tuberculous. As these experiments have, however, generally been performed in infectious localities, they are not of such great value as might be at first thought, particularly as some observers, Chauveau among others, have rendered animals tuberculous by making them swallow the sputa of phthisical patients, or the flesh and milk of tubercular cows.

Thus the question is still *sub judice*, and if in this manual tuberculosis, syphilis, and glanders are grouped together, it is less in consideration of their infectious character than on account of the anatomical characters of their morbid products. Syphilis and tuberculosis have in fact one essential difference, in that the former determines, in its initial stage, productive inflammation (or plastic as was said formerly) resulting in the formation of adult tissue, such as connective or osseous tissue; while tubercular inflammation is above all destructive and followed by mortification, as may be seen in caseous or tubercular pneumonia, enteritis, laryngitis, &c.

The coincidence between the peculiar inflammation of tuberculosis and granulations struck Niemeyer, and suggested to him a theory which we cannot admit. Observing what takes place in the intestine and lung, when at the periphery of ulcerations of the intestines and of vomicæ of the lung tubercular granulations are present, and comparing this fact with the caseous state of the lymphatic glands consequent on cutaneous eruptions in children, and the frequency of tubercular granulations in subjects who have caseous glands, Niemeyer concluded that tubercular granulations are always the result of infection of the organism by a caseous focus, even when purely inflammatory in its origin. Thus, according to him, tubercular granulations have no specific cause, any focus of acute or chronic inflammation in the caseous state may be the cause. But this theory, stated in an absolute manner, wants but a single contradictory fact to destroy it; and there are many observations of general tuberculosis, collected precisely by those observers who sought for and were anxious to find caseous foci, Virchow and Buhl for example, in which they have not been discovered; and we might cite others made by ourselves. Miliary tuberculosis is primary in such cases, and hence there is no reason to think but that it is generally so, or, at least, that granulations and inflammations may develop at the same or different points of the organism excited by the same disease.

Description of tubercle.—The tubercular or grey granulation appears to the naked eye as a little nodule varying in size from $\frac{1}{20}$ mm. to 2 or 3 mm. in diameter; the latter size is rare; it is hard, prominent, transparent if recent, but soon becomes opaque and yellowish at the centre; it is generally surrounded by a reddish vascular zone. These characters are not absolute and may not always be found; when the granulations are confluent they form yellowish masses, impossible to distinguish with the naked eye from inflammatory caseous foci. Moreover, when tubercle develops in a mass of inflammatory tissue, as may be frequently observed in serous membranes, in the pleura and peritoneum for example, though they may be solitary it is impossible to distinguish them, with the naked eye, from the surrounding embryonic tissue. Hence it is seen that tubercle may be discrete or confluent.

The cellular elements constituting a tubercular granulation, are difficult to isolate from a tissue so dense, dry and compact. By scraping and teazing, small fragments and variously formed cells are obtained, and sometimes large cells containing a great number of nuclei,—the giant-cells of German authors; often also fusiform and embryonic cells, but the elements which predominate are small cells, measuring 4 μ to 9 μ in diameter, the nuclei of which are surrounded by a very small amount of protoplasm. These are embryonic cells undergoing atrophy. The reciprocal arrangement of these cells is important. In a section of a granulation, a peripheral zone of proliferation may be recognised containing large mother-cells and fibroplastic elements. This zone is sometimes much more extensive than might, at first sight, be supposed; in the centre the elements are closely packed together, they atrophy as they grow older and finally break down into a granular detritus (fig. 109). Around all these elements a

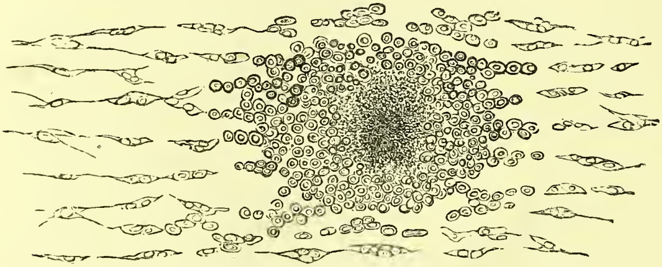

Fig. 109.—Tubercular Granulation.

From Virchow's 'Cellular Pathology.'

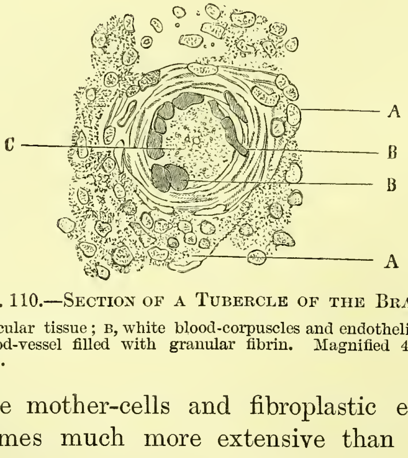

Fig. 110.—Section of a Tubercle of the Brain.

A, tubercular tissue; B, white blood-corpuscles and endothelial cells; C, blood-vessel filled with granular fibrin. Magnified 400 diameters.

granular or fibrillar ground substance is produced which agglomerates and binds them close together. As the result of atrophy and molecular destruction, the centre of the little nodule becomes friable and opaque.

The blood-vessels are never permeable at the centre of a granulation; examination shows that this obliteration is brought about slowly. If studied in a delicate section of tubercle (fig. 110) the outline of the vessels can be made out and they are seen to be filled with a coagulum of granular fibrin. In the midst, and particularly on the border of the granular contents, white blood-corpuscles (*b*, fig. 110) are found, distinguishable from adjacent cells belonging to the tubercular granulation by their larger size and regular arrangement in a circular manner within the walls of the vessel. Now there is an accumulation of leucocytes along the vascular walls every time that the blood-current slows. This proposition results from experiments made on the web of a frog's foot, in which, if an incision be made, the vessels obliterated at the point of incision form culs-de-sac, where the circulation passes slowly; these diverticula in which the blood-current slows become filled with leucocytes, for the impulse of the current is not sufficient to overcome the adhesive property of the white corpuscles. As, on the other hand, white corpuscles are not more numerous in tuberculosis than normally, we are obliged to admit that slackening of the blood-current, shown by the accumulation of the

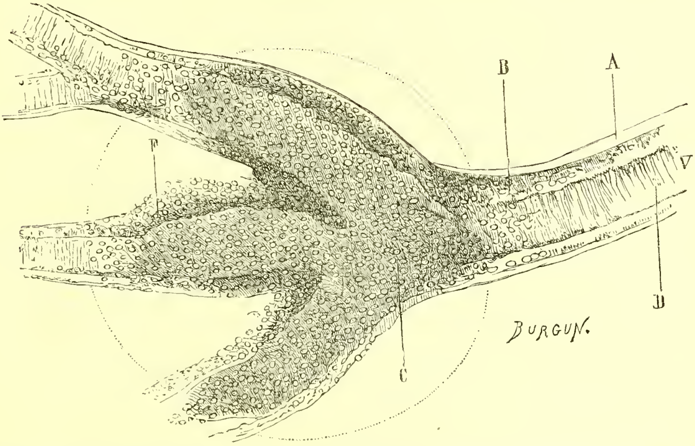

FIG. 111.—ISOLATED VESSEL OF THE PIA MATER PASSING THROUGH A TUBERCULAR GRANULATION, THE LIMITS OF WHICH ARE INDICATED BY THE DOTTED LINE.

A, lymphatic sheath; B, vascular wall; F, proliferating elements of the adventitious coat of the vessel; C, coagulated fibrin in the interior. Magnified 100 diameters.

leucocytes along the walls of the vessels, has preceded coagulation, and arrest of the circulation.

In sections of tubercle obtained after hardening in alcohol, round or irregular granular masses are generally found in the granulations or at various points; at the periphery of these masses are oval nuclei stained red with picro-carminate of ammonia, while the granular substance is stained orange-yellow. This staining allows, even with a low power, of the recognition of these masses; they are the **giant cells** of the Germans. The frequency of giant cells in tubercle induced Schüppel to look upon them as the characteristic element of tubercle, but they are nothing of the kind, as they are met with in other pathological products, notably in all caseous masses of whatever source, provided that the pathological evolution has been slow. These large cells can be isolated by macerating a portion of tubercle in a 33 per cent. solution of alcohol. They are of irregular shape, granular at the centre, and send out branching processes; they may be compared to the

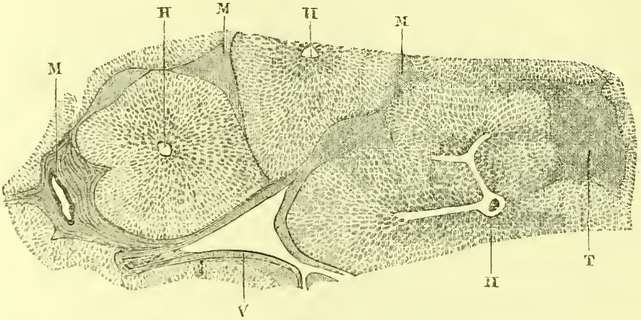

FIG. 112.—SECTION OF LIVER CONTAINING TUBERCLE.

H, H, central veins of the hepatic lobules; M, M, interlobular connective tissue thickened and embryonic; a tubercle, T, is seen in the midst of this tissue; V, section of a branch of the portal vein. Magnified 20 diameters.

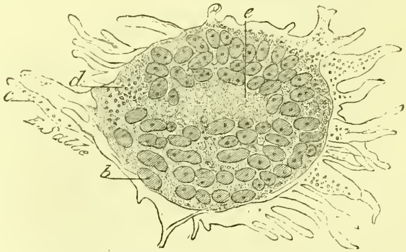

FIG. 113.—GIANT-CELL OBTAINED BY DISSOCIATING A FRAGMENT OF TUBERCLE IN ALCOHOL.

e, granular centre; *c*, processes of the protoplasmic substance which forms the cell; *b*, nuclei. Magnified 250 diameters.

mother-cells of the medulla of bone. Owing to their position and shape it has been thought that these cells are developed in the interior of vessels or at all events in their walls; it may even be possible that they are a variety of vaso-formative cells. Such is the interpretation given by MM. Malassez and Monod after a research which they made on these elements in sarcoma. The question requires fresh investigation. In the first edition of this book we did not regard them as cells, but as fibrinous plugs formed in the interior of the vessels. The obliteration of vessels is constant in tubercle, and the fibrinous coagulum including cellular elements closely resembles a giant cell. According to some observers, Cohnheim in particular, giant cells are lymph cells placed under exceptional conditions of nutrition; indeed, in chronic inflammation lymph cells may acquire a considerable size and form true giant cells, like those observed in tubercle. Sometimes though not attaining the size of large giant cells, they may be called small giant cells. The constant and essential fact is that tubercles have no permeable blood-vessels.

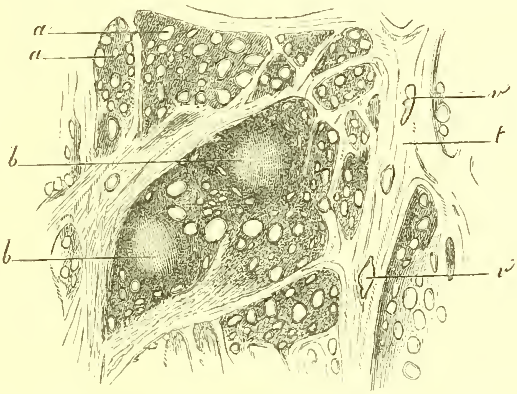

Fig. 114.—Section of the Thyroid affected with Tubercle.
a, alveoli of the thyroid; *t*, fibrous trabeculæ; *v*, vessels; *b*, *b*, tubercles. Magnified 20 diameters.

Development of tubercle.—Tubercle is developed in the midst of embryonic tissue, so that tubercular granulations are always surrounded by a zone of proliferating cells. They are often developed from the connective tissue of organs; in the liver, the granulations develop from the interlobular tissue and are always preceded by interstitial hepatitis (fig. 112); in the bones, tubercle is preceded by ostitis, that is to say, by the formation of embryonic tissue in the medullary spaces. It may be asked if it is not possible for tubercle to develop equally well from connective tissue, the medulla of bone, or epithelial cells? Colberg and Rindfleisch have decided this question in the affirmative as regards the pleura and peritoneum; and in the thyroid body we have observed the epithelial cells contained in the alveoli proliferate and most unquestionably take part in the formation of a tuberculous nodule. In the adult the thyroid gland is composed of alveoli, lined with pavement epithelium, and containing colloid material. In the development of tubercle of the thyroid body, the epithelial cells are seen to multiply (fig. 115) and press on the central colloid mass (*d*, fig. 115) until it is finally entirely absorbed. The alveoli of the gland are then filled with new and small cellular elements (F, fig. 115), at the same time the interalveolar connective tissue proliferates, and the whole constitutes a mass of embryonic tissue in which the nodule of tubercle is developed. In the lung, tubercle may be developed from the interlobular, peri-bronchial and interalveolar connective tissue, but more frequently the tubercular granulations are seen to occupy the centre of many alveoli, the elastic septa of which have been preserved. The embryonic tissue springs from the inner wall of the alveolus, the lining epithelium of which taking an important part in the production of the new tissue; it is certain also that in the alveoli there is an

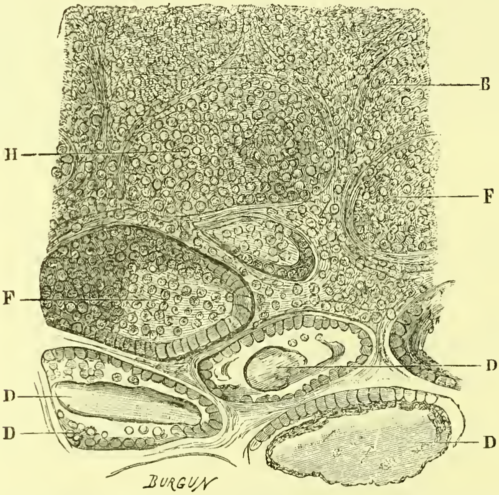

FIG. 115.—PERIPHERY OF A TUBERCLE OF THE THYROID.

D, thyroid alveoli with the epithelium normal, and with colloid masses in the centre; F, alveolus, the cells of which have proliferated, the colloid mass having almost entirely disappeared; at H the alveolus is no longer recognisable except by the arrangement of the fibrous tissue at its periphery; it is filled like the adjacent connective tissue with new cells, B, which are atrophied in proportion as the centre of the granulation is approached.

accumulation of white blood-corpuscles which reach them by diapedesis; so that tubercle seems to be formed from very different elements; from connective-tissue cells, lymph cells and epithelial cells. Tubercle develops in an analogous manner in the thyroid body, the lungs and the medulla of bones.

On **the structure of tubercle** a great variety of opinions has been put forward. Förster classifies tubercle among tumours of lymph cells, that is to say that the cells of tubercle resemble those of the lymphatic glands, which is equal to saying that they are small and round; other observers have adopted this view, though since Donders, Kölliker, His, and Frey asserted that reticulated stroma was the chief characteristic of lymphatic tissue, it is more difficult to regard tubercle as composed of new lymphatic tissue. Rindfleisch, it is true, has described a reticulated stroma in tubercle, but after the description given by himself and after our own observations made to verify its exactness, we affirm that there is in tubercle no true reticulated stroma similar to that of the lymphatic glands, and that the appearance of a reticulum is due to the action of hardening reagents on the intercellular substance. Virchow considers tubercle to be a lymphoid product, while gummata are formed of a tissue similar to granulation tissue. But in fact gummata and tubercle have essentially the same histological constitution, and the same mode of development; both are formed of small cells surrounded by fibrous tissue, and in our opinion they are both species of fibroma composed of nodules of cells of which those at the centre undergo atrophic degeneration.

Varieties of tubercle.—Tubercular granulations are either discrete, or form by their union distinct masses the size of a pea, hazel-nut, or walnut; if developed on a surface, such as a serous membrane, they form more or less extensive plaques. Discrete tubercle is surrounded by a zone of proliferation in which blood-vessels, often dilated, are present; this red vascular zone renders the tubercle, which is anæmic, semi-transparent, or opaque, much more apparent. Confluent tubercles are often massed in great numbers; they are held together by a framework of embryonic tissue. The centre of each tubercle is atrophied in the same way as that of gummatous nodules, but in the former the blood-vessels are soon obliterated, those of the neighbouring embryonic tissue becoming so later; from which it results that the granulations, no longer separated from one another by vascular tissue, are blended together and form an anæmic mass, in which it is impossible, with the naked eye, to recognise separate centres, and the whole mass soon softens and becomes uniformly opaque. In the lung, similar caseous centres are often spoken of, even by distinguished observers, as caseous pneumonia (the infiltrating tubercle of Laennec); but the lung is not the only organ in which these masses of tubercle may be observed; they may be studied in bone, where they have often been confounded with the caries called by the Germans atonic caries; further, every osseous lesion with a caseous appearance has, in the absence of microscopic study, been called tubercular. Hence, a confusion of opinion regarding tubercle of the bone, some observers denying its existence, others seeing it everywhere, which confusion we shall hope to remove when studying osseous lesions. Round, irregular or flattened masses of confluent tubercle may also be observed in the kidney, supra-renal capsules, lymphatic glands, intestinal mucous membrane, and serous membranes, &c.

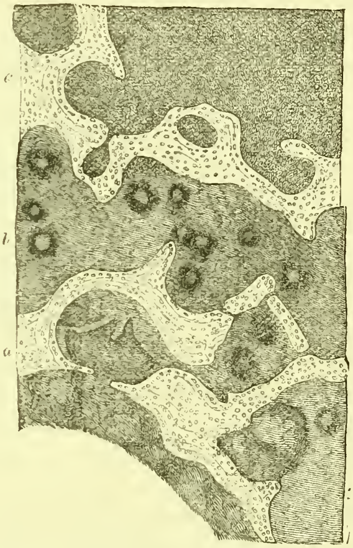

Fig. 116.—Transverse Section of the Body of a Lumbar Vertebra affected with Confluent Tubercular Granulations.

a, osseous trabeculæ; *e*, embryonic medullary tissue; *b*, tubercular granulations. Magnified 20 diameters.

Modifications and secondary lesions of tubercle.—Tubercle does not seem to be capable of absorption like softened syphilitic gumma. The cicatrisation which follows is always the result of mortification, and elimination by ulceration. However, isolated foci are often found in the apices of the lungs, filled with a caseous or almost solid calcareous substance, and surrounded by indurated tissue; but it is often impossible to determine the origin of such foci which might as well be the remains of infarcts, abscesses, or dilatated bronchi separated from the rest of the air-passages, as cicatrised tubercular cavities.

Tubercle frequently undergoes *fibroid degeneration.* At the apex of the lung, in the midst of interstitial pneumonia, little hard nodules may, for example, be found composed of homogeneous fibrous tissue and containing a small number of round atrophied cells; these nodules do not generally contain blood-vessels, and their form, arrangement, and the intermediate states observed between them and typical tubercles leave no doubt as to their nature. They seem to be tubercles arrested in their evolution.

Caseous degeneration is usual in old tubercular granulations. This character is so essential that no hesitation need be felt as to the tubercular nature of a small nodule, the centre of which is opaque and yellow and in a state of caseous degeneration. Granulations which are semi-transparent throughout their entire mass may, on the contrary, be confounded with other neoplasms of inflammatory origin, or with carcinoma, fibroma, sarcoma, &c. Caseous degeneration is generally attributed to obliteration of the blood-vessels; this explanation is natural, but as caseous degeneration occurs in gummata in which the blood-vessels are permeable (see p. 193), it is one that is open to doubt. The caseous degeneration of tubercle causes their death and softening.

The progress of the process of elimination by inflammation is extremely variable; it is generally very slow and irregular, and varies according to the seat of the tubercle, the organs affected, and the constitution of the subject. Thus, in the bones, tubercle causes suppurative ostitis, and in the lung, cavities are the most common results; in the liver, on the contrary, tubercle never causes suppurative inflammation; in the lymphatic glands, tubercular granulations sometimes determine, as in the bones and lungs, foci of suppuration, but generally, as in the liver, the adjacent tissues tolerate the new growth, which ultimately undergoes complete caseous degeneration ending in petrifaction. As regards the personal conditions of the patient, though knowledge is incomplete on the subject, it is known that bad hygienic conditions, insufficient food, unhealthy dwellings and excessive labour favour suppurative inflammation.

From what precedes it is evident that the progress of inflammation around tubercle causes very varying lesions in the surrounding tissues; in the bones, if tubercle is confluent, there is necrosis, and besides the suppurative inflammation which is the local consequence, there are, at variable distances from the focus of suppuration, rarefying or condensing ostitis in the bone or under the periosteum, or hyperostosis. In the lung, the lesions accompanying tubercle are catarrhal, fibrinous and interstitial pneumonia ; these different forms of pneumonia are present alone or united in the same subject in both lungs or even in the same lung, side by side with discrete or confluent granulations in various states of evolution. These tubercular masses act on the surrounding living tissues like foreign bodies, often producing ulcerative inflammation around themselves, and the formation of a focus which may open into a mucous canal, such as a bronchus, the intestine, or epidydimis. By softening, the same result is brought about and cavities are produced. If the tubercular mass remains enclosed in parenchymatous tissue it dries and undergoes calcareous degeneration. The fat is decomposed into fatty acids, crystallised stearic acid for example, and into cholesterin in the form of rhomboidal plates ; the calcareous granules, at first indistinct, become welded together so as to form hard concretions which may remain in the economy for an indefinite period. But the same series of phenomena is common to infarcts and tumours, so that seeing a calcareous nodule in the midst of some organ it is impossible to say, as is however often done, if it is a degenerated tubercle or not.

Anatomical diagnosis of tubercle.—The diagnosis of solitary tubercle is easily made with the naked eye, but if the tubercles are confluent and form a caseous mass they can only be recognised by means of the microscope, unless there is a zone surrounding the mass in which granulations are distinctly recognisable ; in fact, in tubercle as in all tumours, the centre presents the lesions of the periphery in a more advanced stage ; the proof of which is given on microscopical examination, for tubercular granulations are then recognised in the midst of a caseous mass composed of them. We have often seen the name of caseous pneumonia given to such caseous masses, when an attentive examination left no doubt as to the presence of tubercular granulations. With the naked eye it is sometimes difficult to distinguish between confluent tubercle and syphilitic gummata in process of evolution. In fine sections, however, made after hardening in alcohol or chromic acid, it may be observed that in tubercle all the vessels are obliterated by a granular mass, while in gummata they are empty or contain red blood-corpuscles. When gummata are old and their blood-vessels are also obliterated, they form well-defined, hard, lardaceous, caseous masses, surrounded by a thick, firmly adherent fibrous layer (see p. 197), while the caseous masses resulting from confluent tubercle have not the same solidity, they break down, and are incapable of isolation from the surrounding tissues which have simply the appearances of inflammation.

Prognosis of tubercle.—The grave nature of tubercle is so well known that there is no occasion to insist upon it. It is still a question if tubercle is capable of cure, or if it acts like certain malignant tumours in causing at a distance growths similar to itself. The clinical study of patients followed for a long period of time, considered together with post-mortem examinations, show that solitary tubercular granulations often remain small, undergoing but slight caseous degeneration, for an almost indefinite period in the midst of indurated masses resulting from interstitial pneumonia. At the autopsy of old subjects, isolated, small, rather hard tubercular nodules are also found probably dating back a great number of years, and of which the centre is in a state of caseous degeneration. The curability of this form of tubercle, as well as that which has undergone fibroid change, is manifest. The conditions necessary to bring about this happy termination seem to be that the tubercles should be solitary, or few in number. Confluent tubercle may remain at the same spot for a long time without setting up reaction, but more often it acts as a foreign body producing eliminative inflammation around itself, which may sometimes terminate by cicatrisation and cure. The most serious manifestation of tuberculosis consists in the generalisation and dissemination of tubercular granulations in many organs at once, notably in the serous membranes. The peritoneum and pleura are very often invaded at the same time.

Class VII. Glanders.

In **glanders,** as in syphilis and tuberculosis, there are two orders of lesions, those purely inflammatory and those in the form of nodules. In glanders the nodules are similar to tubercular granulations. Spontaneous in the horse, in man glanders is always the result of equine infection. In man, as in the horse, the disease commences by a tumour, or by a primary ulcer, the *farcinous chancre*, soon followed by lymphangitis and accompanied by abscess, acute or chronic suppuration with discharge of serous pus. When the disease is localised in the skin, blood-vessels, and lymphatic glands, it generally receives the name of acute or chronic farcy. If the disease begins in the air passages, the nasal fossæ, the larynx, trachea, bronchi, or lung it is called acute or chronic glanders. Glanders, properly so called, and farcy are two manifestations of the same general disease also called glanders, a disease essentially contagious and inoculable.

In the horse, in which we will first study the histological changes of glanders, the disease is characterised by two kinds of lesions, granulations and inflammation, which show a great tendency to become caseous and produce ulcers. In the horse the granulations of glanders—the glanders tubercle of veterinary surgeons—whether studied in the submucous tissue of the air passages, in the lungs, serous membranes, or connective tissue of the skin, always present the same constant characters, which greatly resemble those of tubercular granulations in man. When, either solitary or confluent, the granulations are situated in the nostrils and project on the surface of the mucous membrane, they soon cause desquamation of the epithelium, and slight superficial ulceration and catarrh. On microscopical examination these granulations are found to consist of an accumulation of embryonic or lymph cells, those at the centre being atrophied and in a state of granular degeneration, while those at the periphery are in a state of active development. In the lungs, if situated in the connective tissue adjacent to a small bronchus, they often encircle it like a complete ring (fig. 117); intense catarrh and ulceration of the bronchus are the consequence of this peri-bronchitis; at the periphery of a similar glandular nodule there is pulmonary congestion and pneumonia, and the pulmonary alveoli are found filled with lymph cells and red blood-corpuscles. But the granulations are not always situated around a bronchus, more often they occupy an entire infundibulum; the alveoli of the infundibulum are then filled with embryonic cells held together by a granular substance, while the epithelial cells have disappeared (see Renaut, art. *Morve*, in the *Dict. encyclo. des sc. méd.*). The nodule is surrounded by a more or less extensive zone of lung tissue in which the alveoli are filled with blood. The nodule soon undergoes caseous degeneration and suppurative inflammation, from which cavities result, similar in the horse to those produced by pulmonary tuberculosis in man.

The granulation of glanders is formed of small cells contained in a partially fibrillar substance; the elements which are at the centre atrophy and soften from granular fatty degeneration. It is difficult to distinguish these growths, produced by glanders in the horse, from tubercle in man.

In man, glanders may show itself by acute symptoms, by catarrh, special inflammation of the air passages, cutaneous pustules and multiple abscesses situated in the subcutaneous connective tissue and in the muscles; accidents rapidly terminated by death, or succeeded by the more localised symptoms of acute or chronic farcy. The small foci in various organs are similar to those observed in purulent infection. In a case under the care of M. Hérard[1] we ascertained that the little nodules of the lung, trachea, and larynx, instead of being similar to the glanders granulations of the horse, did not differ from the abscesses of purulent infection. The larynx and trachea simply showed small submucous abscesses, and the lung areas of metastatic, lobular pneumonia. The pustules of the skin did not differ notably from those of variola, the diffuse suppuration of the subcutaneous cellular tissue was identical with cellulitis, and the abscesses of the muscles presented nothing special.

M. Kelsch has since published a histological examination of the lesions observed in a subject who died from glanders, and like ourselves, he saw in the lung small centres of suppurative pneumonia, and in the mucous membranes and skin, small miliary abscesses. In an autopsy recently made on a patient of M. Hayem, at the Hospital of St. Antoine, it was the same. The preparations of cutaneous pustules which we made in this last case showed us that, compared with the pustules of variola, the difference consisted in the suppuration commencing in the corium and subcutaneous connective tissue, instead of in the Malpighian layer as in variola. (For fuller details see the 'Pathological Histology of the Skin.')

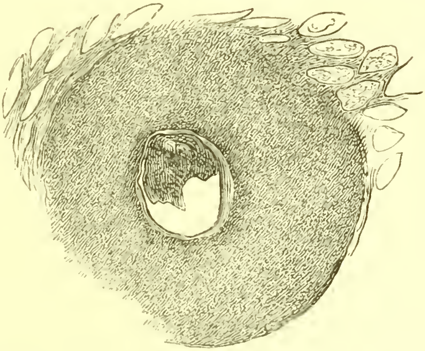

FIG. 117.—SECTION OF A GLANDERS NODULE FROM THE LUNG OF A HORSE.

The tissue of the growth forms a regular ring round a small bronchus. Magnified 40 diameters.

Prognosis.—Death is the rapid and invariable termination of acute glanders; this is in consequence of dissemination and generalisation of the granulations; but chronic farcy and even acute farcy may be cured if the lesions are superficial and are energetically treated from the beginning.

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[1] For fuller details see the case published by M. Carville in the *Gazette des hôpitaux*, August 25, 1868.

III. TUMOURS HAVING THEIR TYPE IN CARTILAGINOUS TISSUE.

Chondroma.

Definition.— Formerly all tumours which presented the physical characteristics of cartilage were called chondromata; but we have eliminated certain tumours which resemble cartilage with the naked eye, but which are nothing of the kind, such as the lamellar fibroma described above (p. 164). On the other hand, true chondroma does not in the least resemble with the naked eye typical, that is to say, hyaline cartilage.

Chondromata being composed of cartilage, their definition is subordinate to that of the cartilaginous tissue. Certain cartilaginous growths, called ecchondroses and developed only from pre-existing cartilage, should from the beginning be distinguished from chondromata. They are found on the articular cartilages and are generally multiple and developed in consequence of inflammation (see chronic rheumatism and white swellings): also on the costal cartilages at their union with the bones cartilaginous nodules are sometimes observed, the result of rachitis, to which the name of ecchondroses has also been given. Virchow describes as ecchondroses the little cartilaginous masses found on the thyroid cartilage and tracheal rings.

Description.—Chondroma, properly so called, is never developed from pre-existing cartilage. Every variety of cartilage, previously described (p. 17), is met with in chondromata, and also a variety which does not exist physiologically in man, but which is found in the cephalic cartilages of the cephalopods. In these animals, the cartilage cells are not enclosed in a capsule, but they have processes by which they anastomose together (*vide* fig. 119). The ground substance surrounding them is of a cartilaginous nature. On observing the mode of development of this variety of cartilage, it is seen that the capsules which, primitively, envelop the cells, are pierced by anastomotic processes sent out to adjacent cells. The facility with which the capsules and ground substance are pierced is truly remarkable. Later, the capsules become indistinct and disappear. This variety of cartilage of the cephalopods has its exact analogue in certain chondromata ; hence the necessity of describing it.

In the adult, cartilaginous tissue is deprived of blood-vessels, and it is the same in most chondromata ; but a cartilaginous tumour may become vascular for a limited extent as far as the centre, while new layers of cartilage are deposited at the periphery. The part of the cartilaginous lobe which has been pierced by blood-vessels accompanied by connective tissue, is transformed into an embryonic tissue similar to the medulla of bone ; the tumour is finally reduced to a cartilaginous shell containing medulla and blood-vessels.

It is rare for a chondroma to be formed of one lobe, particularly if of large size, there is generally an union of many distinct cartilaginous masses, separated by connective tissue. These masses are usually spherical, though sometimes of irregular form and variable in size ; in the same tumour, some being no larger than a pin's head and others as large as a pigeon's egg. It may happen also that all the lobes of a tumour have not the same structure, some may be formed of hyaline cartilage, others of mucoid cartilage, some of fibro-cartilage and others again of cartilage with ramifying cells. These various lobes are generally covered by a fibrous membrane which acts as a perichondrium and in which the vessels ramify ; beneath it there is a layer of lenticular capsules flattened horizontally, more deeply, the capsules are globular, and in the centre there are large capsules containing many generations of secondary capsules. It is in chrondroma that the largest capsules are found.

Varieties of chondroma.—The differences between chondromata are not very marked, but the tissues of which they are composed and the modifications these tissues undergo furnish bases for a classification of varieties of chondroma :—

(*a*) *Unilobular, hyaline chondroma* is formed simply of a single lobe of hyaline cartilage covered by a fibrous membrane ; on the surface are lenticular capsules and at the centre capsules similar to those of permanent cartilage in the adult.

(*b*) *Multilobular, hyaline chondroma* consists of a certain number of lobules similar to the preceding and separated by connective tissue.

(*c*) Sometimes the lobules of the latter variety are separated by vascular fibro-cartilage.

(*d*) In other cases, side by side with well-organised cartilaginous centres are found masses, of variable size, of embryonic tissue, sometimes mixed with fibrous tissue and embryonic cartilaginous tissue. We do not think with Virchow, that these tumours should be looked upon as chondro-sarcoma, for the embryonic tissue round the cartilaginous centres is simply the matrix whence new cartilaginous tissue is formed, and represents the first phase in the development of cartilage.

(*e*) The fibrous tissue which separates the lobules of cartilage sometimes predominates ; it may be either purely fibrous, or fibro-cartilaginous. Virchow makes a distinct species of this tumour under the name of chondro-fibroma ; but we look upon it only as an important variety, for fibrous tissue constantly enters into the constitution of chondroma.

(*f*) When chondroma is developed in glands, particularly in the parotid or testicle, glandular ducts and culs-de-sac, the cells of which are proliferating, are always found in the fibrous tissue separating the cartilaginous islets. Is it permissible to call chondroma of the glands adeno-chondroma ? We think not, for proliferation of the cellular elements of glands in consequence of a neighbouring irritation is a secondary, accessory fact, observed in every kind of tumour developed in glands. In chondroma, as in other kinds of tumours, proliferation of the epithelial cells of the glandular acini is followed by the various forms of degeneration of these cells ; moreover, if a chondroma, developed in a gland, spreads beyond the latter, it contains no acini in its extra-glandular portion. Chondroma of the parotid, for example, whatever may be its course of evolution, contains glandular acini, the cells of which proliferate and form, by their agglomeration, solid epithelial cylinders. It is not for all that epithelioma or carcinoma. These chondromata may be dangerous on account of their situation, and the size which they sometimes attain, but they never cause secondary growths.

(*g*) A certain form of chondroma developed in bone may form an elevation on the surface, while covered by a layer of bone ; this layer extremely thin and wanting at places is always covered by the periosteum. It is generally admitted that this layer is produced by a new formation of bone in consequence of periosteal irritation ; but it is not proved, and it may as well be due to the bone in front of the tumour being pushed forward, as shown in the experiments of Duhamel on the interstitial growth of bone.

(*h*) The cartilaginous tissue of chondroma may produce osseous tissue. It has generally however only a transitory existence, as we shall see *à propos* of development. This form is called *ossifying chondroma.*

(*i*) Some chondromata are not formed of lobules, but of a diffuse mass often presenting the characters of embryonic cartilage.

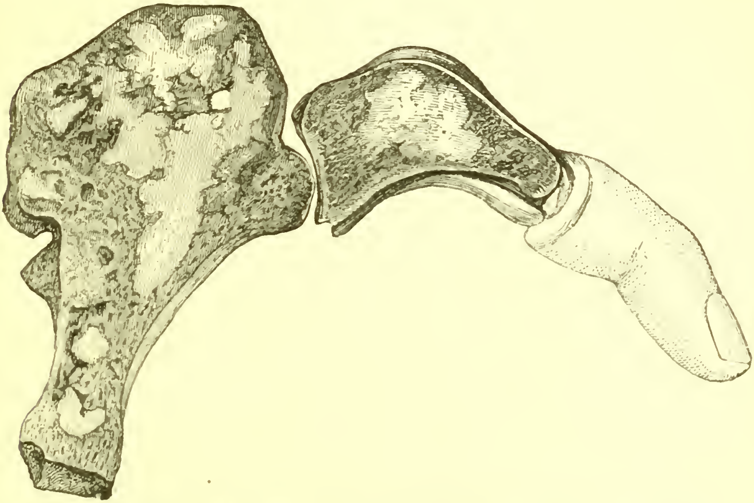

Fig. 118.—Diffuse Chondroma of the Metacarpus and Phalanx.

Figure borrowed from the 'Surgical Pathology' of Nélaton.

This variety which is generally met with in bone is called *diffuse chondroma.*

(*j*) The lobules of some lobulated chondromata may at their centre undergo mucoid degeneration. Sometimes the cartilage capsules are preserved and are free in a mucoid substance, as in the intervertebral disks; in other cases the cellular elements are destroyed. The lobule is then transformed into a cyst of which the

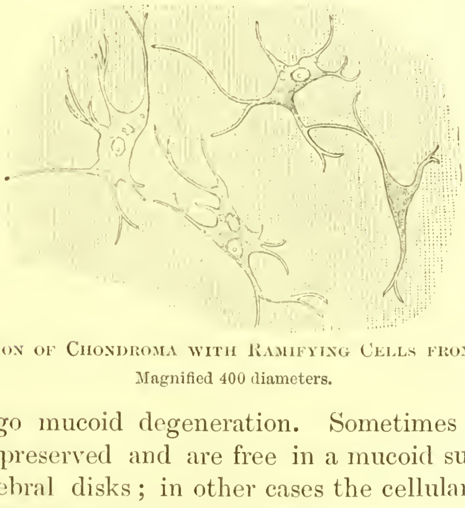

Fig. 119.—Section of Chondroma with Ramifying Cells from the Parotid.

Magnified 400 diameters.

wall is cartilaginous; this is *cystic chondroma*, the cysto-chondroma of Virchow.

(*k*) Sometimes chondroma, notably that of the parotid gland, is formed partly or wholly of cartilaginous tissue with ramifying cells like that of the cephalopods; we call it *chondroma with ramifying cells* (fig. 119).

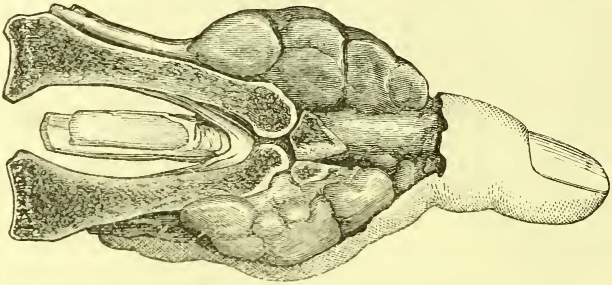

Fig. 120.—Perichondroma of the Phalanges.

(*l*) Generally these different forms of chondroma are variously combined, and in reality most chondromata are mixed.

Seat of chondroma.—Chondroma, as we have already said, never springs from cartilage. It may be located in all the organs, but it develops by preference in the bones, in the parotid, testicle, skin, subcutaneous cellular tissue, muscles, lung, &c. In the *bones* it is generally developed in the central medullary canal of long bones or in the medullary spaces of spongy bones; it is then called *enchondroma*. Enchondroma varies, it may be lobular or in diffuse masses, hyaline, fibro-cartilaginous or with ramifying cells, &c. When superficially seated, it is covered by an osseous shell, or is in direct relation with the periosteum, which

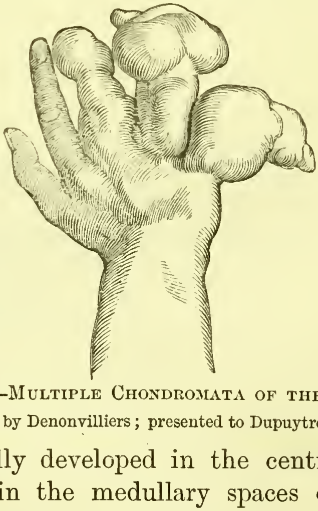

Fig. 121.—Multiple Chondromata of the Fingers.

Preparation by Denonvilliers; presented to Dupuytren's Museum.

itself sometimes becomes cartilaginous. Chondroma is occasionally developed under the periosteum and at its expense, the bone taking no part in the formation of the morbid mass; it is then called *perichondroma.* Chondromata of the extremities are sometimes enchondromata, sometimes perichondromata, often the two forms are united. In *glands*, very complex forms of chondroma are met with, the different varieties of cartilaginous tissue are often found mixed. The tumour develops from the connective tissue between the acini and the glandular ducts; the epithelium contained in the acini and ducts proliferates and is finally destroyed, undergoing various retrograde metamorphoses. In the *muscles*, the connective tissue alone takes part in the new formation; the muscular fasciculi undergo fatty degeneration, atrophy and disappear, after showing multiplication of their nuclei.

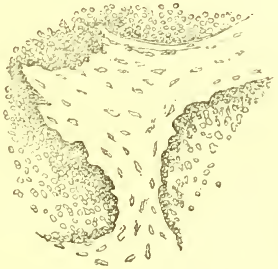

FIG. 122.—DEVELOPMENT OF A CHONDROMA IN OSSEOUS TISSUE.

The osseous lamellæ are cut into festoons, the spaces filled with embryonic tissue. Magnified 50 diameters.

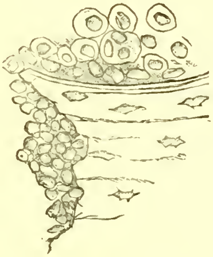

FIG. 123.—THE LEFT CORNER OF THE PRECEDING FIGURE IS HERE REPRESENTED MAGNIFIED 300 DIAMETERS.

The embryonic cells are becoming changed into cartilage cells.

Development and ulterior modifications of chondroma.—Chondroma is not developed direct from adult tissue, but only after the latter has returned to the embryonic state. If developed in osseous tissue, phenomena similar to those of ostitis are first observed; the cells of the medulla and the adipose cells proliferate, and the embryonic cells thus produced are soon separated from one another by a transparent substance. The adjacent osseous trabeculæ are festooned and the spaces formed are filled with embryonic cells (figs. 122 and 123). In the oldest part of this embryonic tissue the cells are kept wide apart by a transparent and cartilaginous ground substance; so that a small centre of cartilage is formed in the midst of an enlarged medullary cavity; around this centre of cartilage the embryonic cells proliferate and the process of conversion of bone into medulla is carried on at the same time that the osseous trabeculæ are absorbed, so that adjacent medullary cavities communicate and form one large cavity in the centre of which are formed one or more cartilaginous nodules. These enlarge by the inclusion of surrounding embryonic cells; later, the adjacent embryonic tissue is changed into fibrous tissue and constitutes a true perichondrium; the peripheral capsules of the cartilaginous island then flatten and become lenticular, while the cells at the centre become round and multiply, so that secondary cells and capsules are produced within the primary (fig. 124). The same phenomena occur when chondroma springs from connective tissue; the connective-tissue cells multiply, the fibres soften and dissolve, and islets of embryonic cells are developed from which cartilage develops in the ordinary way. In some cases, if development is slow, the fibrous ground substance persists, the cells become encapsuled, and fibro-cartilage is produced. Well-defined cartilaginous islets, surrounded by a perichondrium, grow by the multiplication of their cells. The elements of these islets are generally very large and allow of all the phases of multiplication being followed; the nucleus is seen to enlarge, elongate and become constricted at the centre till complete segmentation is effected; each of the two nuclei is then surrounded by a distinct mass of protoplasm, and each new cell secretes around itself a secondary capsule.

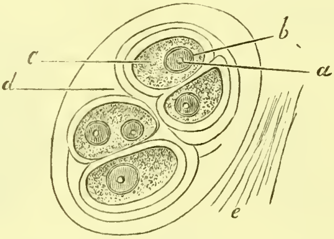

Fig. 124.—Cartilage Cells in Process of Proliferation.

a, nucleolus; *b*, nucleus; *c*, protoplasm; *d*, primary and secondary capsules; *e*, ground substance.

Chondromata undergo nutritive changes from their very beginning; thus if growth is rapid, the cells are infiltrated with a glycogenic substance, which acted upon by iodine turns orange-brown. When once fully formed the cells and ground substance of chondromata undergo various changes; if growth is stationary the cells always contain droplets of fat; sometimes at points where interstitial growth is very marked, the cells are simply infiltrated with glycogenic substance, while at others this substance is replaced by drops of fat. It is possible that there are between these two substances chemical relations which have hitherto escaped our observation. Granular fatty degeneration is sometimes observed in chondroma, it differs from the preceding in that it causes complete destruction of the cartilage cells and an arrest of development of the parts affected. Calcareous infiltration never occurs at the periphery but always at the centre of cartilaginous nodules. It may occur under two different conditions, it either accompanies active formative change similar to ossification, or it is shown, on the contrary, by a calcification which invades all the secondary capsules at the same time. The latter does not differ from calcareous incrustation previously described. In the first case (fig. 125) the process is similar to normal ossification from cartilage; the cells contained in the capsules proliferate, the ground substance splits up, the primary capsules open and the secondary capsules are dissolved; the cells proliferate and form a medullary cavity within the cartilage in which ramify numerous vessels, springing from the perichondrium. Thus far, it is seen, that this new formation of embryonic tissue does not differ

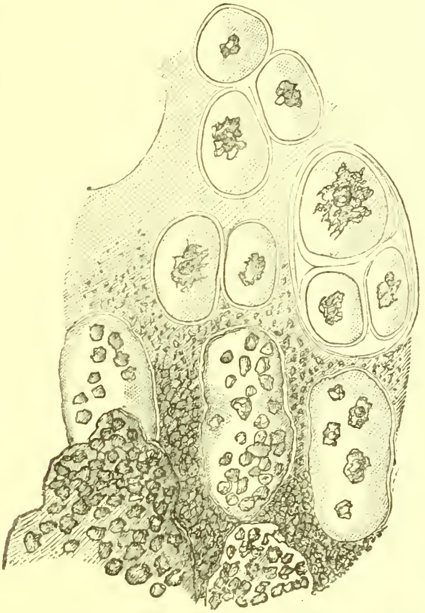

FIG. 125.—CARTILAGINOUS CAPSULES OF CHONDROMA INVADED BY CALCAREOUS INFILTRATION.

In the calcified portions at the lower part of the figure, the cells have multiplied and become embryonic. Incomplete decalcification in chromic acid. Magnified 300 diameters.

from that preceding physiological ossification; but in chondroma the medulla may: (*a*) remain embryonic; (*b*) give origin to fibrous tissue; (*c*) be transformed into an adipose tissue like the medulla of long bones; (*d*) become the point of departure of osseous trabeculæ, which have only a temporary existence and which often disappear to give place again to medulla. If a section be made through the whole thickness of a chondroma formed of a single cartilaginous nodule it will show, if examined from the periphery towards the centre: 1, the connective tissue of the perichondrium; 2, a layer of hyaline cartilage; 3, a layer of cartilage in process of proliferation; 4, in the centre an irregular cavity filled with medulla and furrowed by trabeculæ of calcified cartilaginous tissue or by osseous lamellæ. Thus, it is seen, that the centre of the tumour is the seat of a process effecting the disappearance of the cartilage, and if new cartilaginous elements were not constantly formed beneath the perichondrium, all the old cartilage would disappear in consequence of a process which we may call *medullization.*

Prognosis.—In considering the prognosis of chondroma account must be taken of the mode in which the tumour has developed. If the morbid mass is well defined and surrounded by a dense fibrous tissue, a true perichondrium, and if it develops solely at the expense of its own elements, its gravity is slight; but if surrounding the tumour tracts of embryonic tissue and cartilage undergoing development are found, if, in fact, there is no fibrous perichondrium, the gravity is greater. A relapse is sometimes observed after extirpation, and even secondary growths in one or more organs far removed from the primitive mass. It is hence impossible to assert that chondromata are benign tumours, for some of them closely resemble carcinoma and sarcoma in the course they pursue.

Osteoid tumours.—Under the name of osteoid tumours or osteoid chondromata J. Müller has described tumours formed of a tissue analogous to bone, but not presenting actually all its characters. Virchow is more definite. In studying the development of bone, which he did in the rachitic bone of children, he examined the particular tissue called by Rufz and J. Guérin by the name of *spongeoid*, and renamed it *osteoid tissue*, considering it to be osseous tissue in the course of physiological development. We are here obliged to anticipate the subject of rickets, which is described later on more in detail, in order to explain the nature of this osteoid tissue. Under the periosteum, in rachitic bone, a tissue similar to that of bone is often found, in the ossiform trabeculæ of which, instead of finding bone corpuscles and parallel lamellæ, angular corpuscles are seen in a ground substance, which may be homogeneous or have distinct calcareous granules scattered through it. Instead of being separated by a medullary tissue, these trabeculæ are in the midst of a fibrous tissue well supplied with blood-vessels (fig. 126). Virchow supposed that this tissue, to which he gave the name of osteoid, existed physiologically beneath the periosteum, and he looked upon it as the first phase in the development of osseous tissue, and he gave the name of osteoid to those tumours exclusively formed of it. This hypothesis of Virchow has been completely reversed by modern researches, but Virchow's description of osteoid tissue is still correct as regards rachitic bone and osteoid tumours.

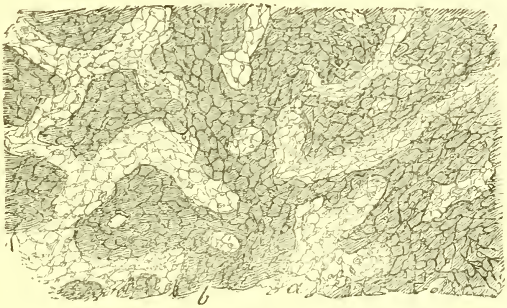

Fig. 126.—Sub-periosteal Osteoid Tissue in Rickets.

a, osteoid trabeculæ; *b*, medullary spaces filled with fibrous tissue.

An osteoid tumour is therefore composed of trabeculæ, varying in size and form, and formed of a substance which may be refractive and homogeneous, or vaguely fibrillar and often infiltrated with calcareous granules; these trabeculæ contain angular corpuscles, and they are separated from one another by fibrous tissue in which the blood-vessels ramify. Osteoid tumours are, however, not entirely composed of such a tissue, they almost always contain scattered centres of cartilage, and they are infiltrated in places with calcareous salts. It is only when islets of cartilage are developed in the tissue adjoining the osteoid trabeculæ, that the name of osteoid chondroma should be used. In some parts of these tumours calcareous infiltration is almost always to be found; solitary granules are deposited in the ground substance of the trabeculæ, but the cells which are surrounded by this deposit are not for all that bone corpuscles.

There is here simply calcareous infiltration or complete petrifaction, and the corpuscles never show but few and incomplete processes. The ground substance also never becomes laminated.

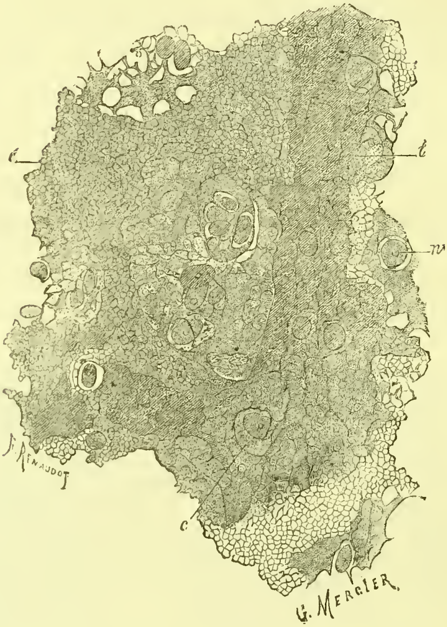

Fig. 127.—Tissue of an Osteoid Tumour of the Lung observed by M. Lannelongue.

i, calcified trabeculæ containing cells included in a calcareous and granular mass; *n*, cell contained in a cartilaginiform shell in the fibrous trabeculæ. Magnified 200 diameters.

An osteoid tumour is generally diffuse, but it sometimes forms a single mass, or it may be lobulated, never, however, in such a

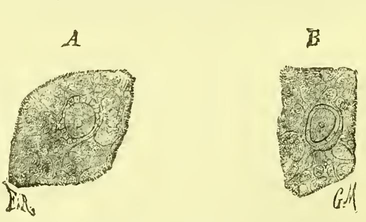

Fig. 128.—Cells with their Cartilaginiform Shells contained in Fibrous Trabeculæ.

Magnified 300 diameters.

marked degree as ordinary chondroma. It has no limiting fibrous membrane analogous to the perichondrium.

It may attain a great size; the prognosis is grave, and secondary growths may be developed in a great number of organs. Virchow lays great stress on these secondary growths, and we have seen many examples of them. It is a rare form of tumour. With the naked eye it is difficult to recognise, as it closely resembles sarcoma, fibroma, and chondroma, and the intermediate forms of these tumours.

The anatomical diagnosis can only be made from sections, cut after hardening and decalcification by picric or chromic acid. The characters of the osteoid tissue should first be determined, after which the proportion of fibrous or cartilaginous tissue present should be ascertained. It is only by a thorough examination, that osteoid tumour can be differentiated from fibroma or chondroma, to which it is very nearly allied.

IV.—Tumours formed of Osseous Tissue.

Osteoma.

Osteoma is a tumour composed of osseous tissue. The different varieties of osseous tissue previously described (p. 16) may be found in these tumours, and we divide them according to the nature of this tissue into three species.

I. **Eburnated osteoma.**—On the internal surface of the bones of the skull, Virchow found osteomata composed of concentric lamellæ parallel to the surface of the tumour. In the lamellæ, lacunæ were found with canaliculi radiating towards the periphery, as in the cement of the teeth. This form contains no blood-vessels.

II. **Compact osteoma.** — Compact osteoma is composed of osseous tissue resembling that of the diaphyses of the long bones; it is arranged in concentric lamellæ surrounding vascular canals; it is distinguished from the tissue of the diaphyses of the long bones by the Haversian canals being irregular in direction instead of parallel.

III. **Spongy osteoma.**—This form is composed of spongy or even of areolar tissue. The medulla, which forms the largest part of the tumour, may be embryonic, gelatiniform, fibrous, or adipose.

Seat and development of osteoma.—Two groups of osteoma may be distinguished according to the seat of their development. The first group comprehends those connected with bone; the second those which are developed far from bone. I. The former may be formed at the periphery of the bone or in its medullary cavity, and they are thus divided into *exostoses* and *enostoses*.

Exostoses.—In exostoses situated on the surface of bone, the Haversian canals generally run perpendicularly or obliquely to those of the parent bone; the periosteum is raised by the tumour, so that there is perfect continuity between the periosteum of the bone and that of the exostosis. As to the direction taken by the Haversian canals it is easily explained. When in exostosis the sub-periosteal medulla is transformed into osseous tissue, the osteo-periosteal vessels determine the direction of the Haversian canals and the arrangement of the osseous lamellæ; now, as is well known, these vessels are perpendicular or oblique to the surface of the bone. Exostoses are divided into epiphysial and parenchymatous.

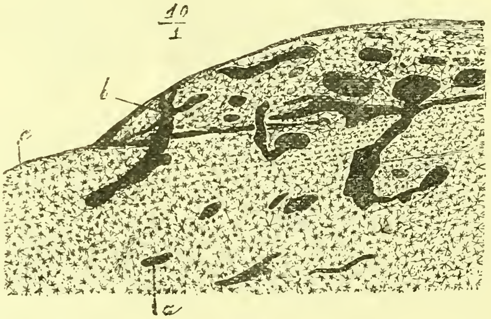

FIG. 129.—SYPHILITIC EXOSTOSIS OF THE OS FRONTIS.

c, lamellæ parallel to the surface of the frontal bone; above is the osseous tumour; the medullary canals and blood-vessels are seen to penetrate the tumour from the old bone. The Haversian canals, stained red with carmine in the preparation, are here shown black. Magnified 10 diameters.

Epiphysial exostosis is met with in the long bones. It may also be found on the surface of the bones of the skull, in which case it is generally related to syphilis. On section, the old and new tissue are seen to be perfectly distinct. In fig. 129, beneath the exostosis are seen the parallel lamellæ of the old bone. Exostoses of the long bones have the same arrangement as those of the skull. They are deposited on the lamellar systems of the old bone without destroying them, and are always developed under the periosteum by the proliferation of the sub-periosteal medulla. The osseous trabeculæ are then formed according to the usual method. In some rare cases an exostosis may be covered by a continuous layer of cartilage from which the osseous tissue is obviously developed. In such a case the periosteum is seen on section to have been changed into perichondrium, beneath which is cartilage, the deep layer of which is proliferating, bone being formed at the centre.

Parenchymatous exostoses develop in the substance of the bone, in the following manner: in consequence of rarefying ostitis, a loss of bone substance is caused, which loss is filled up by inflammatory medullary tissue, which tissue becomes the point of departure of a new exuberant growth of bone. In these cases the new bone is easily distinguished from the old. The former is developed around the blood-vessels of the granulations, which spring up on the surface of the initial lesion, from which it results that the Haversian canals of the exostosis have generally a direction perpendicular to those of the old bone. This is shown in fig. 130.

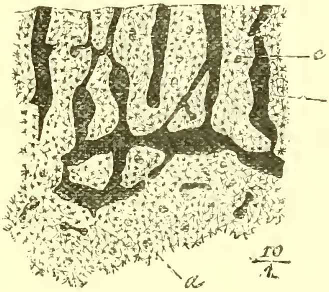

FIG. 130.—SECTION OF A PARENCHYMATOUS EXOSTOSIS OF THE TIBIA PERPENDICULAR TO THE AXIS OF THE BONE.

a, Haversian canals of the old bone cut across; *b*, Haversian canals of the exostosis running in a direction perpendicular to that of the former; *c*, longitudinal canals. Magnified 10 diameters.

Exostoses are developed at all ages; if the patient is still growing they develop in the epiphyses and are then often multiple and symmetrical. Broca made a special study of this variety and called it epiphysial exostosis; Soulier has given it the name of osteogenic exostosis, which very well describes its nature.

Enostoses, generally formed of compact tissue, fill up more or less completely the central canal of the bone.

II. Osseous growths formed outside of the osseous system are not always tumours; we nevertheless describe them here so that they may not be omitted. They develop from various tissues of the organism. Certain cartilages habitually become the seat of osseous metamorphosis, as the effect of old age, particularly the cartilages of the larynx, trachea, bronchi, and ribs. Ossification of the thyroid cartilage is also observed in old persons, and in those who have suffered from laryngitis, particularly tubercular laryngitis; in the latter case, it is due to an inflammatory condition of the cartilage in relation with inflammation of the mucous membrane. In the pathological ossification of cartilage, centres of embryonic tissue are observed, the result of the rupture of the primary cartilage capsules, dissolution of the secondary capsules, proliferation of the free cells, and penetration of blood-vessels. This embryonic tissue is thus seen to be formed by a process exactly similar to that of physiological ossification. Osseous trabeculæ are then developed, in which embryonic cells are transformed into bone corpuscles. At the commencement of this process the cartilage is more friable than normally, for it contains medullary spaces, and the osseous trabeculæ are still delicate; it afterwards becomes as solid as spongy or even as compact bone. The same phenomena of ossification are observed in the cartilaginous rings of the trachea. In ossification of the ribs, frequent in old persons, the process is slower, and is impeded by mucoid degeneration. In the ossified costal cartilages, cysts are formed filled with mucus and the debris of cells incapable of further organisation; a more active process is required for the production of osseous tissue. In joints, affected with chronic rheumatism, osteomata spring from the diarthrodal cartilages and synovial fringes; but the consideration of these new growths belongs properly to dry arthritis and white swellings, and they will be described when treating of these diseases. Osseous tumours may also be developed in tendons; in which case they originate at the point of insertion in the bone, in the form of long needles or stalactites reaching sometimes as far as the muscle. In the connective tissue of the dura mater, arachnoid and pia mater, little plates are often observed, composed either of connective tissue incrusted with calcareous salts, or of true osseous tissue. In subjects who have been long blind, the choroid may be transformed into a bony shell formed of osseous lamellæ and corpuscles. We lately observed osseous tissue in the wall of an old cyst of the liver in a case presented to the Society of Anatomy, by M. Pelvet. Bones have sometimes been found in the midst of muscles; and Rokitansky has described osteomata, found rather frequently, in the biceps of wrestlers and in the adductors of the thighs of the cavalry soldiers of the Austrian army. Veritable osseous plates are also found in the pericardium and even in the muscular tissue of the heart; but most of these are really cases of lamellar fibroma incrusted with calcareous salts. As to the calcareous plates formed in blood-vessels affected with chronic endoarteritis, though Virchow considers that they are of an osseous character, we assert that they possess neither osseous lamellæ, medulla, nor true bone corpuscles. The irregular slits and small cavities met with in them have neither the form nor the canaliculi of true bone corpuscles. In the skin, osseous tissue is sometimes produced around the glands. Virchow stated this fact, and we have ourselves once had occasion to observe it. In the indurated apex of tuberculous lungs osseous growths are pretty frequently met with; they take the form of needles or radiating masses and have been often described. They were thought to originate from the bronchial cartilages; we have however succeeded in tracing their development and have ascertained that they spring from the new connective tissue of interstitial pneumonia. The osseous trabeculæ circumscribe irregular spaces or are developed in the form of tubes. At first sight, the latter might be mistaken for small bronchi with ossified walls, but on studying sections cut after decalcification in

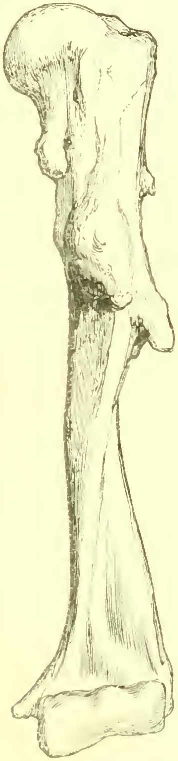

Fig. 131.—Exostoses of the Humerus at the Point of Insertion of the Deltoid.

Figure borrowed from the 'Surgical Pathology' of Nélaton.

chromic acid, the central canal is seen to be filled with marrow which is even often adipose. These formations are really long bones in miniature. Besides osteomata of the arachnoid and pia mater, the central nervous system may be the seat of osseous tumours developed in the nervous tissue itself; as, for instance, in the centre of the cerebrum or cerebellum. We have seen one such case in the latter organ.

When considering osteoma, **odontoma,** a tumour formed of one of the dental tissues, should be mentioned. Under the title of odontoma, a name given by Virchow, are included not only tumours of the teeth, but those of the neighbouring tissues; they are as follows:—

I. Exostoses caused by inflammation of the alveolo-dental periosteum. The teeth, as is well known, are composed of a central pulp and of ivory or dentine; the free surface of the tooth is covered by enamel, and the root by cement. This cement, a true osseous tissue, is in direct relation with the periosteum of the alveolus, and consequently in inflammation of the periosteum, new layers of cement, that is to say, new osseous layers are produced.

II. New growths of enamel and ivory either at the neck of the tooth, or on the cement. These little tumours resemble drops of wax stuck on the surface of the tooth.

III. A peculiar tumour of the maxilla, formed of one or more normal or deformed teeth, sometimes welded together, or grouped in consequence of some congenital vice of formation. Under the name of odontoma very different things, as we see, are included; and to them should be added, according to Virchow, the teeth implanted in osseous plates, met with in dermoid cysts. Odontomata are never large, nor are they serious, and their pathological importance is not great.

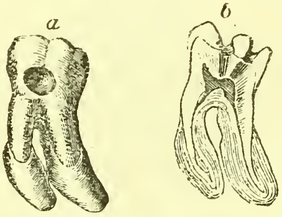

FIG. 132.—DENTAL EXOSTOSIS.

a, surface; *b*, section of the tooth. Figure borrowed from Virchow's 'Pathology of Tumours.'

V.—TUMOURS FORMED OF MUSCULAR TISSUE.

Myoma.

The definition of myoma is suggested by that of muscular tissue itself. Muscles are divided into three groups:—

I. The striated muscles of the animal system.

II. The cardiac muscle.

III. The non-striated muscles of the organic system.

Muscular tissue of the second group has never been observed in tumours, but the two other varieties of muscular tissue, enter, unequally it is true, into the formation of tumours; hence two kinds of myoma may be distinguished:—

I. Tumours containing striated muscular fibres. Zenker has given these the barbarous name of *rabdo-myoma*, for which it seems to us well to substitute the name of **myoma of striated fibres.**

II. Tumours formed of non-striated muscular fibres, the *leiomyoma* of Zenker, and which we call the **myoma of smooth fibres.**

Myoma of striated fibres.—This is often a congenital tumour; there are but few recorded cases; the first case, published by Rokitansky, was that of a congenital tumour of the testicle of the size of a pigeon's egg; it was mostly formed of striated fibres. Billroth has since published a similar case. Virchow and Recklinghausen have observed in the cardiac muscle of new-born children, tumours containing striated fibres, and which they have considered to be myomata. But as these children were syphilitic, Virchow has reconsidered his first opinion and seems now disposed to regard them as gummata. In Lebert's third variety of dermoid cysts, bundles of striated muscle fibres are often met with. In a sarcomatous tumour of the testicle, M. Talavera recently found a notable number of striated muscular fasciculi undergoing development. Some of these fasciculi, composed in the centre of a protoplasmic cylinder containing nuclei, encircled at the periphery by a thin striated layer, were analogous to the muscular fasciculi of a human embryo at three or four months. In this case it seems therefore, that the muscular elements were recently developed from the embryonic cells of the morbid mass. Striated muscular fibres are also observed in other solid tumours developed in the fœtus and described further on; but such morbid masses cannot be looked upon as myomata, for they are composed of a great variety of tissues, and hence merit a special description.

Myoma of smooth fibres.—This tumour sometimes forms an irregular diffuse mass, at others it is well defined. In appearance it is fleshy or fibrous. In myoma, the muscle cells are the same as in the physiological condition; they may be grouped in fasciculi and membranes, or isolated in the midst of a fibrous tissue. The bundles are separated by areolar tissue in which the blood-vessels ramify, but they never penetrate into the substance of the muscular fasciculi. To be certain that a tumour is composed of muscular elements, portions should be macerated in a 20 per cent. solution of nitric acid, or in a 40 per cent. solution of caustic potash. The connective-tissue fibres are then dissolved, and the muscle cells set free; they are recognised by their elongated fusiform shape (fig. 133, A). To demonstrate their characteristic nuclei, portions of the tumour should be hardened by the ordinary methods, and sections cut, stained with carmine, and treated with acetic acid. The acid causes the muscular substance to swell and the bundles to become indistinct; the muscle cells with their elongated rod-shaped serpentine nuclei are then easily recognised. In fig. 133, A is from a preparation of uterine myoma, the fibres of which have been dissociated by the action of nitric acid, and B is from a section of the same tumour hardened in alcohol, stained with carmine and treated with acetic acid. Myoma can also be well studied in sections stained with picro-carminate of ammonia, or purpurin. The former stains the muscular fibre yellow, while the connective tissue is rose-coloured. Purpurin does not touch

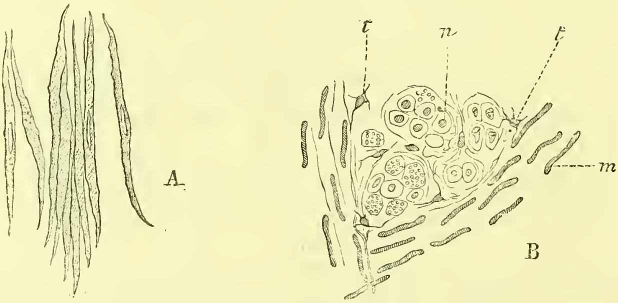

FIG. 133.—MUSCLE CELLS FROM MYOMA.

A, cells isolated by the action of nitric acid; B, from a preparation hardened, stained with carmine and treated with acetic acid; *m*, longitudinal section; *n*, transverse section of nuclei; *t*, connective-tissue cells.

the connective tissue, but stains the body of the muscle cell rose-colour, and the nuclei more or less dark red. Myoma is formed of bundles which are either parallel to one another or intersect in different directions, so that in section bundles are seen to be divided longitudinally and transversely. In the latter case the cells are seen as two concentric circles, the internal of the two, more deeply stained, is the divided nucleus. As, however, the nucleus only occupies a small portion of the fibre, and the fibres are irregularly placed at different levels, it may chance to be avoided here and there in making a section across the fibres, and hence may not always be seen to occupy the centre. This is an important point, as it assists in distinguishing a divided muscular fasciculus from a bundle of nerve tubes or a collection of small cells. In the connective tissue which separates the muscular fasciculi, more or less numerous connective-tissue cells are found in the arteries, veins, and capillaries. An interesting property of myomata is their contractility. Virchow frequently mentions this property, and says that during life their consistence differs much according to the moment they are examined, they being soft when relaxed and hard when contracted. It is in the tumours commonly called uterine fibroids that this fact has been ascertained.

The **development of myoma** has been hitherto incompletely studied, for their progress is slow, and when there are a great number of small myomata located, for example, in the walls of the uterus, the post-mortem examination may be made at a time when they are stationary, and the study of their development impossible. Sometimes, however, collections of embryonic tissue may be met with in the fibrous tissue and along the muscular bundles of the tumour. The contractile cells may be developed in the same way as in the embryo, by direct transformation of embryonic cells. Some observers have thought that pre-existing muscle cells produce new ones by multiplying by division (Förster); but we consider that new tissue always results from the new formation of muscle cells, and not from the hyperplasia of pre-existing muscle cells, for, as with most of the fixed cells, neither division of the nucleus nor segmentation is ever seen in the muscle cell.

Myomata may be divided into the following varieties; I. *Non-lobulated myoma* formed of a homogeneous fleshy mass, soft to the touch, with the muscle cells large, and the fasciculi generally having all the same direction. 2. *Lobulated myoma*, this has sometimes large, gaping blood-vessels, like the uterine sinuses and hepatic veins. In some rare cases the dilatation of the blood-vessels may be so great as to cause hæmorrhage; in which case the myoma is called erectile. 3. *Calcareous change* is frequent in myoma and begins in the centre of the lobules. There is sometimes only calcareous infiltration of the cementing substance, at others complete petrifaction both of this and the muscular fibres, either at the centre of a lobule or throughout its whole mass. This degeneration is very frequent, particularly in those tumours of the uterus which project into the peritoneal cavity. 4. *Fatty degeneration* of the cells of myoma is sometimes present side by side with calcareous change. 5. *Mucoid degeneration* is often associated with dilatation of the blood-vessels. It causes the destruction of a certain number of elements and the formation of cavities or mucous cysts, described by Cruveilhier under the name of 'geoda.' These cysts, met with sometimes in uterine myomata, contain mucus, cellular detritus, and sometimes blood proceeding from ruptured vessels lining the cyst.

Seat of myoma.—Myoma of smooth fibres is found in regions where this form of muscular tissue exists. It is most frequently met with in the *uterus*, where it is either interstitial, lobulated, and encysted in the substance of the uterine tissue and capable of enucleation, or projecting under the peritoneum or into the uterine cavity. The two last-mentioned commence by being interstitial, but they advance either towards the peritoneal or the uterine cavity, covered by the peritoneum or the uterine mucous membrane. Myoma of the uterus is either formed of pure muscular tissue, or of muscular tissue mixed with connective tissue. When the muscular elements are insignificant in number and connective tissue predominates, the tumour might be considered to be a fibroma, if in the nomenclature of tumours the commonest tissue was not subordinated to that which gives the morbid mass its special characteristics. Muscular tissue is of new formation in uterine myoma, which is proved by the fact that some myomata developed in the uterine walls contain more contractile elements than the whole uterus. We are therefore unable to think with Rindfleisch that the muscular elements are accessory in these tumours, and, like Virchow, we look upon them as myomata. In old age, the *prostate* is often the seat of a new formation of unstriped fibres, which may cause a total or partial hypertrophy of the organ, or circumscribed tumours. Myoma of the *scrotum* has also been observed (Virchow, Förster). We have examined a case of myoma of the *labia majora*, removed by Demarquay. Balzer recently presented to the Biological Society (Paris) a very interesting case of multiple myomata of the *skin*. Polypoid myomata (Rokitansky) have been found in the *digestive tract*, in the lower part of the œsophagus, the stomach and small and large intestine. These myomata, like those of the uterus, are primarily interstitial but at the end of a variable time they become pedunculated, and form polypoid projections, either into the visceral or into the peritoneal cavity. Some, no larger than a pea or almond, and often multiple, have been found in the substance of the walls of the *stomach*. On isolating them, it may be seen that they are developed from a muscular fasciculus with which they are continuous at the two extremities.

The **anatomical diagnosis of myoma** is impossible without recourse to the microscope. Whatever may be the method employed of making the preparation, myoma is easily recognised under the microscope. In doubtful cases recourse must be had to dissociation of the muscle cells by nitric acid.

The **prognosis of myoma** is not grave, at least so long as by its size or seat it causes no lesions of neighbouring tissues or organs, or presents no obstacle to the performance of the functions of important organs. Thus myoma of the uterus may compress the bladder or rectum, or cause uterine congestion and hæmorrhage; or pedunculated myomata of the intestine may give rise to symptoms of intestinal strangulation.

VI.—TUMOURS FORMED OF NERVOUS TISSUE.

Neuroma.

A neuroma is a tumour composed of nervous tissue of new formation. Normally there are two varieties of nervous tissue: 1, the ganglionic tissue containing nerve cells and found in the grey matter of the brain, spinal cord, and sympathetic system; 2, fasciculated nerve tissue, composed of medullated fibres and of non-medullated fibres of Remak, found typically in the peripheral nerves. These two varieties of nervous tissue constitute two forms of neuroma: 1, medullated or ganglionic neuroma; 2, fasciculated neuroma.

1. **Medullated or ganglionic neuroma** is very rare, and clinically unimportant. Virchow describes tumours of this kind as making slight projections on the surface of the brain and spinal cord.

They must not be mistaken for hernia of the spinal cord which is seen when the pia mater is torn off in removing parts of the cord. Neuroma is of the colour of grey matter, and is composed like it of nerve cells and blood-vessels; it may be found in the corpora striata and on the surface of the ventricles. Sangalli has described tumours formed of grey matter as existing in congenital encephalocele. In Lebert's third variety of dermoid cysts, masses of grey nerve substance are found containing nerve cells, these will be described when considering cysts.

2. **Fasciculated neuroma.**—At the beginning of this century Odier, of Geneva, designated every tumour situated along the course of a nerve as a neuroma; such a tumour is, however, more generally of a myxomatous character as has since been ascertained; but surgeons still continue to apply the name neuroma to every tumour of whatever kind situated on a nerve; though according to the nomenclature at present adopted by anatomo-pathologists, the name should be limited to a tumour formed of nerve elements. By fasciculated neuroma we understand a tumour simply composed of nerve fibres of new formation. The name of *neuroma dolorosum* has also been given to small subcutaneous tumours by reason of the acute pain they cause. Dupuytren called them *fibroma dolorosum.* They probably contain nerves enclosed and compressed in new connective tissue. According to Axmann, they are nested concentric layers of fibrous tissue which he compares to the corpuscles of Pacini; this view has not been verified. Virchow proposes to give them the name of *neuromatia.* We do not see the advantage of this new word, inasmuch as the tumours are very well designated by the name fibroma dolorosum. Under the name of *cylindrical plexiform neuroma* Virchow has described a very interesting variety of neuroma, seated on the course of a peripheral nerve, and characterised by an abundant new formation of non-medullated nerve fibres, and of fibrous tissue between the tubes, so that the nerves increase considerably in size while preserving their cylindrical shape. It is not known if in these cases there is actually a new formation of the fibres of Remak. If these tumours are not accompanied by an actual new formation of nervous elements they are not neuromata.

Fasciculated neuroma is very rare. It is always seated on the track of a nerve, and consequently is in every case a tumour developed in a tissue analogous to itself. It is generally small and uni-lobular. On section, the tissue appears fibrous; it is dry, and on microscopically examining the detritus obtained by scraping, droplets of myelin are observed. A few nerve tubes can be isolated by dissociation with needles ; but if after hardening the tumour in a solution of chromic acid sections be cut, stained with carmine, treated with absolute alcohol, and examined in the essence of turpentine, nerve tubes are seen in great numbers, intersecting in every direction, and separated by connective tissue more or less rich in cellular elements. Virchow has divided neuroma into two distinct varieties, according as it is composed of medullated or non-medullated fibres, and he calls the first *myelinic neuroma*, and the second *amyelinic neuroma* ; the former always contains a variable number of Remak's fibres.

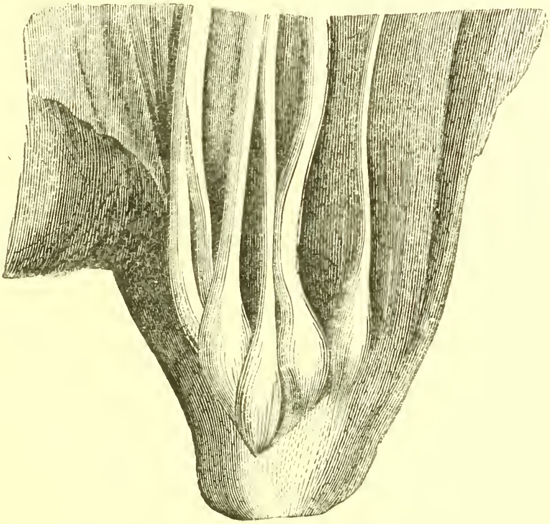

FIG. 134.—CLUB-SHAPED TERMINATIONS OF NERVE-ENDS IN A STUMP.

The **seat of neuroma** is very variable. The most interesting variety of this tumour is found in *stumps* after amputation. The end of the divided nerves become the point of departure of small globular tumours, which might be thought at first to be caused by a simple increase of fibrous tissue. Valentin and Lebert have found in these tumours a large number of medullated fibres. On dissection it is found that each nerve bundle terminates by a small nodal swelling ; on dissociating one of the latter, it is found, on microscopical examination, to be formed of interlacing nerve tubes, sinuous or in loops. It is difficult to ascertain if these convoluted tubes of the nodule are continuous with those of the divided nerve, but it is very probable. The dense fibrous tissue which separates the tubes binds them also together and makes dissociation and isolation of the nerve fibres difficult; in sections also from hardened preparations it is impossible to follow a nerve tube for a sufficient distance to ascertain its relations. We have learnt, however, from experiments made on animals, that the nerve fibres of the proximal end of a divided nerve may give origin to a very large number of nerve fibres of new formation, the arrangement of which is irregular and the course complicated (*vide* chapter on Nervous Tissue). It is consequently very probable that the convoluted nerve fibres, found in the terminal nodules of nerves in stumps after amputation, result from a new formation of nerve fibres, emanating from the old fibres and directly continuous with them.

Neuroma may be also formed apart from traumatic causes in the *course of a nerve.* It is then contained within the connective-tissue sheath of the nerve and forms little nodosities, in which nerve tubes are convoluted as in the terminal neuromata of divided nerves. Instead of being solitary, neuromata are often very numerous along the course of a nerve and its ramifications, or on a plexus, or along all the nerves of a considerable part of the body; such are the *rosary neuromata* of Lebert. The symptoms they cause depend upon the function of the nerve on which they are seated. Thus, neuromata of the auditory nerve may cause deafness; certain tumours of the optic nerve, called neuromata, but which are, according to Virchow, myxomata, have caused blindness. Some neuromata may acquire a considerable size, and extend far along the course of the nerve. These, first mistaken by Virchow for fibromata, have since been described by him as amyelinic neuromata. This kind is not easy to study, indeed it is very difficult to dissociate the fibres of Remak when they are mixed with dense fibrous tissue; recognition is however impossible without isolation, for in sections the tubes may be mistaken for other anatomical elements.

The **anatomical diagnosis of neuroma** is difficult, for the reasons just stated, when a non-medullated tumour is under consideration, but easy in the case of a medullated tumour. For a tumour to be really a neuroma it is not enough for it to contain nerve tubes, but the number of these must be so considerable as to leave no doubt that there has been a new formation of nerve elements.

Prognosis.—Neuromata are generally serious on account of their situation and of the pain they cause, sometimes by reason of their number; but they are incapable of producing secondary growths in other parts of the body.

VII.—Tumours composed of Blood-vessels.

Angioma.

The type of angioma is found in the vascular system. It has been called an erectile tumour by Dupuytren, and angiosis and ecchymoma by Alibert. To merit the names of tumour the vessels composing it must be of new formation. Simple dilatation of old vessels cannot be considered an angioma, nor can an aneurism, nor a hæmorrhagic focus, whatever may be its seat or extent, nor varices and dilatations of the veins with hypertrophy of the venous walls. Virchow describes, under the name of *angioma racemosum*, the dilatations of small arteries, the arterial varices of Breschet, but these are not true angiomata, for there is no new formation of arteries; they are simply dilatations.

We distinguished two species of angioma.

1. **Simple angioma,** in which the newly formed blood-vessels constituting the tumours are similar to normal arteries, veins, and capillaries.

2. **Cavernous angioma,** in which the blood circulates in a lacunar system similar to the cavernous system of the erectile organs.

Simple angioma (*congenital nævus, telangiectasis*) appears as a flat, slightly projecting or polypoid tumour, which is sometimes effaced, at other times swollen. It is red or violet, and is generally seated in the face, round the orbit or on the neck. Simple angioma essentially consists of newly formed capillaries presenting regular ampullar or cirsoid dilatations. The vessels are disposed in a corkscrew or tortuous manner; on section their walls are seen to be rich in nuclei, and are from one to two hundredths of a millimetre in thickness, while preserving the simple structure of the wall of a capillary. The blood-vessels are generally supported by a fibrous or cellulo-adipose stroma, for angioma is usually located in the corium or subcutaneous tissue. Congenital angioma is very common. According to observations made by Depaul, one third of the children born at the Clinic of the Faculty of Medicine at Paris, come into the world with congenital nævi, which in most cases disappear spontaneously during the first months of life.

2. **Cavernous angioma** (*Nævus cavernosus*, *erectile tumour*, *hematode fungus*) is formed of an erectile tissue, the cavities of which are filled with blood. The tissue is hollowed by alveoli which communicate with one another in a very irregular manner, much in the same way as the alveoli of carcinoma intercommunicate. The blood circulates in this cavernous system which takes the place of capillaries, situated as it is between the arteries and veins. The circulation is active, as is proved by clinical observations of the sudden variations of the volume of these tumours; and as we shall see histology confirms this opinion. In angioma may be studied—1. The *septa* limiting the alveoli. They are formed of dense fibrous tissue in which, in sections made after hardening in alcohol, no cellular elements can at first be distinguished; but on treating the preparation with acetic acid and staining with carmine, they become apparent. These trabeculæ may also contain smooth muscle cells or even striated muscle fibres, if the tumour be developed in one of the muscles of the extremities. In the septa, adipose vesicles are also sometimes met with and blood-vessels proper to them, a kind of vasa vasorum, and in one case Esmarch discovered nerve filaments. 2. The *endothelium* which lines these cavernous cavities. It consists of flattened endothelial cells of fusiform shape, if seen isolated and sideways; they are similar to the endothelium of the veins. 3. The blood contained in the cavernous spaces is quite normal, and similar to that which circulates in the rest of the vascular system. If after removal of such a tumour it be cut into, all the blood escapes and nothing remains but a kind of sponge which collapses. If such a tumour, situated on the surface of the liver, be opened, though it may have been hard and prominent, it becomes soft and flaccid and converted into an irregular, wide-meshed network. If, on the contrary, the blood coagulates *en masse*, which occurs if the tumour be placed entire in absolute alcohol, a magnificent natural injection of cavernous angioma is produced. In sections of a tumour thus prepared and hardened, the blood can be examined in the same condition as it existed at the moment of death, and the state of the circulation ascertained. With a power magnifying 200 diameters the trabeculæ, alveoli, and their contents consisting of red corpuscles may be seen, the red corpuscles, as frequently occurs after hardening in alcohol, taking a regular polygonal form ; a few white corpuscles are present and by staining

with carmine, they may be counted, and it is then seen that they are few in number and are not adherent to the septa. These two facts, the small number of the white corpuscles and their non-adherence to the vascular walls, indicate the activity of the circulation in the tumour; for owing to the adhesive property of white corpuscles, a strong impulse of the blood current is necessary to prevent them stagnating along the vascular walls. The facility of circulation in cavernous angioma is proved, moreover, by clinical observation during life. Angiomata are, in fact, erectile, and distension by afflux of blood is produced by emotion, exercise, &c. When the tumour is inflated with blood, pulsation may be distinctly perceived, a phenomenon met with in erectile tissues. The name of erectile tumour, given to angioma by Dupuytren, is apparently therefore well chosen; but all cavernous angiomata are not erectile, and moreover a tumour which has been erectile for a certain time may cease to be so; thus, the name cavernous angioma expresses a constant anatomical condition, and defines the tumour better than a name which expresses a passing and inconstant physiological state.

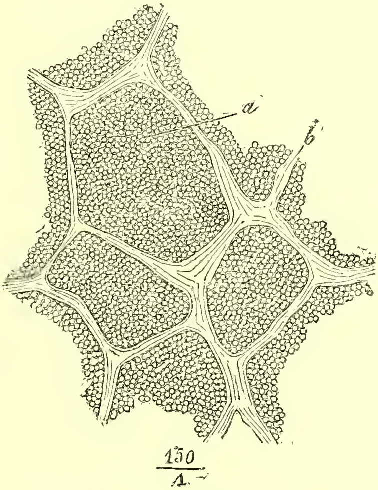

Fig. 135.—Cavernous Angioma of the Liver.

(Section after hardening in alcohol.) *a*, cavernous spaces filled with blood; *b* fibrous trabeculæ bounding the cavernous spaces.

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With regard to **the development of angioma**, Rokitansky admitted that the areolar tissue is developed first, outside the vascular system, and only communicates with the blood-vessels at a later stage. He compared the initial alveolar tissue of angioma to that of carcinoma, and considered that their development was analogous. Luschka, having at the same time observed that blood cysts are found along the course of the cerebral blood-vessels without communication with the latter, used these facts in support of Rokitansky's opinion as to the origin of angioma; but we know, at the present time, that the blood cysts, described by Luschka, are nothing else than dilatations of the perivascular sheaths. In the active development of angioma, embryonic tissue is first produced, and new capillaries, which at first show simple dilatations; but the dilated capillaries being in contact, wide openings are established between them, resulting in the formation of a capillary system with large cavernous dilatations.

Cavernous angiomata are subject to various changes of nutrition. Their vascular walls may be the seat of calcareous concretions similar to those present in the choroid plexus and angiolithic sarcoma. Cysts filled with serum have been observed by Holmes Coote in angioma; they are caused by the isolation of a vascular bud and subsequent metamorphoses of the contained blood.

Can angioma develop into carcinoma or sarcoma? J. Müller reports cases of malignant cavernous angioma with a tendency to increase and produce secondary growths. These must certainly have been sarcomata or carcinomata with dilated blood-vessels. Pulsatile tumours, often regarded by surgeons as erectile tumours, aneurisms of the bone, &c., are nothing else, in fact, but sarcomata or carcinomata with much dilated blood-vessels. Angioma is sometimes diffuse, not separated from the surrounding tissues by an exact boundary, sometimes circumscribed and it may even be surrounded by a true capsule; it is then called encapsuled angioma.

Seat of angioma.—According to its seat cavernous angioma is divided into external and internal.

External angioma of the skin is situated in the corium or subcutaneous cellular tissue. Virchow calls it *lipogenous* if developed in adipose tissue and *phlebogenous* if developed at the expense of the vasa vasorum of the veins. It may extend into the cellular tissue around or within the muscles and even into the bones. Angioma of the mucous orifices, the lips, for example, is called *fissural* by Virchow.

Internal cavernous angioma is observed in the liver, kidneys, and spleen; it is most common in the *liver*. Angioma of the liver varies in size from that of a nut to the half of the hepatic organ; but though it projects on the surface of the liver, it does not generally increase the size of the organ, for it develops at the expense of the hepatic substance. If encapsuled the capsule is pierced by vascular openings. Surrounding the tumour the hepatic parenchyma is normal, but separated from it by a zone of proliferating connective tissue. It is here, when the tumour is extending, that the embryonic walls of the blood-vessels dilate, open into one another, and form, in fact, a new mass of cavernous tissue which communicates and joins with the first. Such a tumour has been known to rupture into the peritoneum and cause peritonitis. Sometimes angiomata shrink after spontaneous coagulation of the blood which they contain, and undergo cicatrisation. Rayer states having observed tumours of this kind in the *kidney*; they have also been seen in the *spleen*. Schuh has published a single but incomplete case of angioma of the *lung*.

Prognosis of angioma.—These tumours have no other gravity than that which results from their situation and extent; they may very well pass unperceived.

The **anatomical diagnosis of angioma** is easy when the vessels and alveoli remain filled with blood; but if the tumour has been divided before being submitted to examination, and the blood has escaped, nothing is left but a collapsed, spongy mass. On drawing the tissue apart with forceps, a system of resisting and elastic septa is seen, which to an experienced observer is sufficiently characteristic of angioma. It might be a question for discussion if such a tumour were not an erectile carcinoma or sarcoma; in such a doubtful case the tissues in the periphery of the tumour should be examined for the characteristic elements of carcinoma or sarcoma. Around and within angioma, only the normal tissues of the invaded part, or embryonic tissue, are found. It might be sometimes difficult to differentiate angioma from myoma of smooth fibres traversed by dilated blood-vessels; but here again the presence of a large number of muscle cells would establish the diagnosis.

VIII.—TUMOURS FORMED OF LYMPHATIC VESSELS.

Lymphangioma.

Tumours formed of newly formed lymphatic vessels may be confounded with simple dilatations of pre-existing vessels. Perhaps the existence of lymphangioma, that is of a tumour composed of lymphatic vessels of new formation, is contestable. Fetzer has described lymphatic, erectile tumours situated in the abdominal walls and in the groin. Some authors, particularly Demarquay, Michel, and Thilesen, have observed similar tumours developed in subjects who have inhabited countries where elephantiasis was prevalent. But there is nothing to prove that these were not simple dilatations of pre-existing vessels. Among lymphangiomata must also be included the tumours described by Nélaton, Trélat, and Anger under the name of *adeno-lymphoceles*, in which the dilatations may be traced to the lymphatic glands.

Lymphangioma is a soft, fluctuating, depressible tumour, adherent or not to the skin. It is composed of a lacework of lymphatics, often communicating with one another as in a cavernous tissue, and they may even open externally and allow the lymph to escape. The histology of lymphangioma is incomplete. Th. Anger has demonstrated that the dilated lymphatic vessels show hypertrophy of their walls, caused by an increase in the number of smooth muscular fibres; he has never been able to make out the epithelium of these dilated vessels.

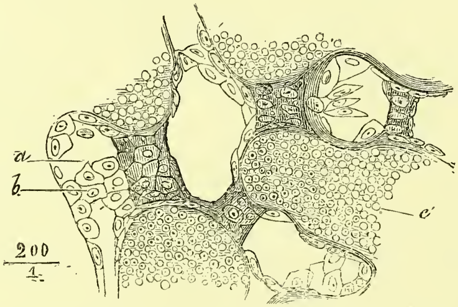

Fig. 136.—Dilated Lymphatic vessels from a Case of Elephantiasis of the Skin of the Penis.

a, lymphatic vessel; *b*, endothelium of the vessel; *c*, embryonic connective tissue of the tumour.

Virchow is inclined to classify congenital hypertrophy of the tongue (*macroglossia*), and of the lips (*macrochilia*) with lymphangioma. In these hypertrophies of the tongue and lips, dilated lymphatic vessels are certainly found, containing a fluid similar to lymph, and located in the midst of a thickened fibrous tissue. In elephantiasis Arabum, in the midst of a succulent connective tissue which constitutes the mass of the tumour, irregular lacunæ are met with full of a fluid resembling lymph. Now it is known that elephantiasis is preceded by recurring angioleucitis, and it is to this that the formation of the lymphatic lacunæ should be referred. We cannot enter into further details concerning lymphangioma, for the authors who have published observations have not made complete examinations; and not having studied the subject ourselves we are not in the position to affirm that there is in these cases a veritable new formation of lymphatic vessels.

IX.—TUMOURS FORMED OF THE TISSUE OF THE LYMPHATIC GLANDS.

Lymphadenoma.

Lymphadenoma is formed of the adenoid tissue of His or retiform connective tissue (p. 15).

In 1845 Virchow and Bennet discovered **leucocythemia,** a disease in which the spleen and lymphatic glands are simultaneously or separately hypertrophied, and the blood contains a large number of white corpuscles. Later, peculiar growths are developed in the liver, kidney, and other organs. In the liver the hepatic cells and lobules are seen to be separated by new, round elements, located in the connective tissue; these cells were considered to be white blood-corpuscles produced by proliferation of the connective tissue, which proliferation was thus looked upon as the point of departure of new white corpuscles. Similar appearances in the kidneys, spleen and lymphatic glands were interpreted in the same manner, and looked upon as the origin of the excessive increase of leucocytes in the blood. Hodgkin had as early as the year 1831 studied a fatal disease characterised by progressive hypertrophy of the spleen and lymphatic glands. It is probable that some of these cases were those of leucocythemia. In 1856 Bonfils discovered that the lymphatic glands and spleen may be hypertrophied, though the blood contain no greater number of white corpuscles than normal, and in these cases of hypertrophy of the spleen and the lymphatic glands without leucocythemia, new growths are also observed in the liver, kidneys, &c. Trousseau called this disease **adenia.**[1] It is known in England by the name of **Hodgkin's disease.** According to our own opinion leucocythemia and adenia form two varieties of the same morbid condition. The essential lesions of the different organs are in fact the same in the two diseases, and these are lymphadenomata, tumours formed of adenoid tissue.

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[1] Adenia, as the name of a disease, is not recognised in the *Nomenclature of Disease of the Royal College of Physicians*, nor does it occur in Ziemssen's *Cyclopædia*, or in our principal text-books of medicine; the disease so named by Trousseau is what is known in England as Hodgkin's disease, or Lymphadenoma. Lymphadenoma is, however, the name of the symptomatic tumour, and does not denote the general condition. 'Hodgkin's disease' is of course memorial rather

The definition of lymphadenoma being based on that of the tissue of the lymphatic glands, we shall commence its study by a description of this tissue. The normal adenoid tissue of the follicles of the lymphatic glands, the corpuscles of the spleen, the closed follicles of the intestine, and similar organs, is characterised by a reticulated connective tissue, the meshes of which are filled with lymph cells. Capillaries traverse this reticulum and are surrounded by a condensed layer of the reticulated tissue. It is in fact from this sheath that the fibres of the reticulum spring. At the points of intersection of the fibrils, and on the surface of the fibrils themselves, endothelial cells are found. In sections, from which the lymph cells have been brushed away, the nuclei only of these endothelial cells are generally perceived. The name of lymphadenoma should only be given to tumours formed of adenoid tissue of new formation, and we do not regard as lymphadenomata certain lesions of the organs accompanying leucocythemia which will be described further on.

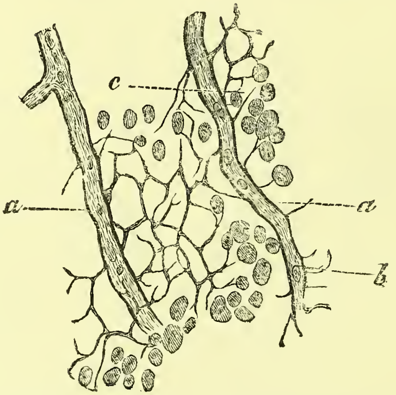

FIG. 137.—RETICULATED TISSUE OF A LYMPHATIC FOLLICLE OF THE INTESTINE. After Frey.

a, capillary blood-vessel, of which the nuclei are visible at *b* ; *c*, meshes of the reticulated tissue containing lymph cells.

than descriptive. I have therefore thought it well to retain in the translation the French name adenia, though unfamiliar to English readers, as it describes better than any of the names hitherto used a disease characterised by a morbid production of adenoid tissue.—[TR.]

Description.—Lymphadenoma is a tumour varying in size from that of a millet seed to that of a fœtal head. It is almost always ill defined in the midst of the organs. In the lymphatic glands it seems to consist of a simple hypertrophy of these organs, but when many neighbouring glands are affected, they melt into a common mass. Lymphadenoma is soft, of a decidedly encephaloid appearance, greyish in colour with red spots which correspond to vascular dilatations or hæmorrhagic foci; parts are sometimes opaque, caseous, and lardaceous. On scraping, a very abundant milky juice is obtained, exactly as in carcinoma. This juice is composed of small, round, uni-nucleated cells, measuring 10 μ in diameter. There are also multinucleated cells measuring 20 μ; some again are still larger and are filled with nuclei. In the parts of the tumour tinted brown or yellow, these cells contain red blood-corpuscles and blood pigment in different stages of decolorisation, such as are found in the spleen. Cells apparently fusiform, but actually flattened and containing oval nuclei, are also found in the juice, they are derived from the endothelium of the vessels or the cells of the reticulate stroma; there are also red corpuscles and free nuclei of various sizes resulting from the rupture of the cells containing them. These various elements, obtained by scraping, give very insufficient notions of the nature of the tumour, and do not differentiate it from encephaloid sarcoma, or carcinoma, from which it is also difficult to distinguish with the naked eye. To recognise lymphadenoma, delicate sections should be cut after

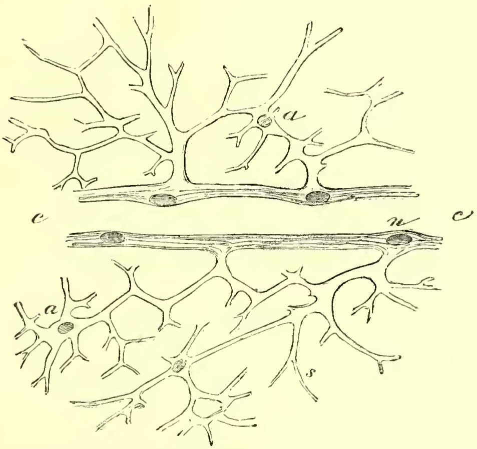

FIG. 138.—TISSUE OF A LYMPHATIC GLAND IN ADENIA.

a, nuclei; s, reticulated stroma; c, capillary blood-vessel; n, nucleus of the capillary. Magnified 500 diameters.

hardening in alcohol, and removing the free cell elements with a camel's-hair brush. The reticulate stroma, the true characteristic of lymphadenoma, then becomes evident,[1] and is distinctly seen to spring from the capillaries (fig. 138). In adenia, if the preparations have been hardened only with alcohol, the blood-vessels appear empty or filled with red corpuscles, which do not stain with carmine. In leucocythemia, on the contrary, the dilated capillaries contain a large number of white corpuscles which stain readily. Capillaries full of white corpuscles are also found in all the organs, so that by this single character leucocythemia, which may have passed unnoticed during life, can be recognised after death.

Seat of lymphadenoma.—When lymphadenoma is developed in the *lymphatic glands* it causes a great increase in the size of the follicles, which are then compressed and modified in form. The connective tissue of the medullary portion of the glands seems to disappear and give place to a hypertrophied cortical substance. On section, the gland has an encephaloid or splenic appearance, and connective tissue can only be recognised at the slits which correspond to the lymph sinuses enveloping the follicles. If after slightly hardening such glands in alcohol or chromic acid a delicate section be cut, and the lymph cells brushed away with a paint-brush, the reticulum is seen united to the capillary vessels. The latter are filled with leucocytes in leucocythemia and with red corpuscles in adenia. The fibrils of the network are two or three times thicker than in the normal condition, their diameter being 2 μ to 3 μ. The gland has everywhere the same structure and is entirely formed of modified cortical substance. The *thymus gland* after having undergone almost complete atrophy may, under the influence of leucocythemia or adenia, recover its original form and acquire a considerable size. In many cases, which we have examined microscopically, we have found adenoid tissue, and we have been convinced that there was here a new formation in the thymus, and not simply hypertrophy of the peri-tracheal glands, for the corpuscles peculiar to the thymus were found. The *spleen* may become modified in the same way as the lymphatic glands. The Malpighian bodies, which in this organ represent the follicles of the lymphatic glands, become hypertrophied out of all proportion, they have been known, indeed, to attain the size of a filbert or walnut. The reticulated tissue shows almost everywhere thickening of the trabeculæ. The capillaries are filled and distended with white corpuscles, if the case be one of leucocythemia. In the *liver* there are many distinct changes. One, which is peculiar to leucocythemia, consists in diffuse extravasation of the white corpuscles. (This was demonstrated by a research carried out by one of us and Ollivier, *Soc. de Biol.* 1866.) The white spots, which in the liver, have been looked upon by all observers as caused by hyperplasia of the connective tissue, is in leucocythemia caused by accumulation of white corpuscles. The hepatic capillaries allow of the escape, with or without rupture of their walls, of a large number of white corpuscles, which are collected in a small limited space or are diffused between the hepatic cells. These undergo fatty degeneration and are soon destroyed. Here, therefore, there is not only development of adenoid tissue but an extravasation of white corpuscles. Besides these foci, there is in the liver a veritable new formation of retiform adenoid tissue. Perhaps the extravasated white corpuscles are the starting-point of this new tissue. In adenia it is almost certain that this is not so, and that the origin of lymphadenoma of the liver must be attributed to hyperplasia of the connective tissue. In adenia we have also constantly noticed a marked enlargement of the liver due to congestion and dilatation of the blood-vessels. These, as seen in fig. 139, are filled with red corpuscles in the midst of which a few leucocytes may be distinguished. In the *kidneys*, there are two kinds of lesions in

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[1] The process of removing all the free cells contained in the reticulate stroma with a camel's-hair brush, is, after hardening in alcohol, both difficult and tedious; the following proceeding will render it easier. A morsel of the tumour suspected to be lymphadenoma is first placed for twenty-four hours in a 33 per cent. solution of alcohol, then into a slightly syrupy solution of gum for twenty-four hours, and then into strong alcohol to complete the process of hardening. After this it is easy to brush away the cells from out of the stroma.

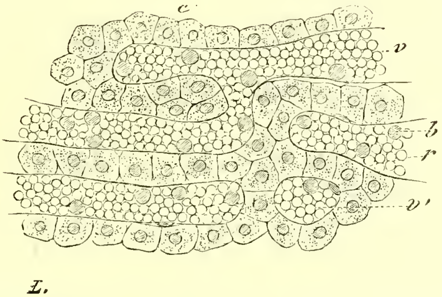

FIG. 139.—TRANSVERSE SECTION OF AN ENLARGED LIVER IN ADENIA.

v, *v*, vessels filled with corpuscles ; *e*, hepatic cells.

every respect similar to those in the liver. There may be extravasation of the white corpuscles and accumulation of them in the capillaries, so that the whole organ looks as if it were infiltrated with pus (fig. 140), or there are true adenoid tumours. Lymphadenomata are frequent in the *mucous membrane of the stomach and intestines*, where they may be almost recognised with the naked eye. They appear like nodular, greyish tumours uniformly coloured or spotted with ecchymoses, they are soft tumefied and convoluted, and ulcerated at the centre; in their neighbourhood the mucous membrane is thickened; on examining with the microscope a section cut perpendicularly to the surface of the mucous membrane, the tumours show the tubular glands filled with granular fatty contents; between and below them there is a reticulated tissue of new formation, characterised by large meshes and thickened trabeculæ. Bœttcher is of the opinion that the contents of the degenerated glands give the reactions of amyloid matter; but in the cases we have examined we have only found granular fatty degeneration. The glands disappear before long leaving nothing but adenoid tissue behind. Lymphadenomata of the stomach have often an extensive surface and measure 3 or 4 c.m. in thickness; when thus voluminous they may be mistaken for tumours of another kind. Their softness, tendency to ulceration, the juice yielded by their surface on section cause them easily to be confounded with encephaloid carcinoma or cylindrical-celled epithelioma, unless a microscopical examination be made.

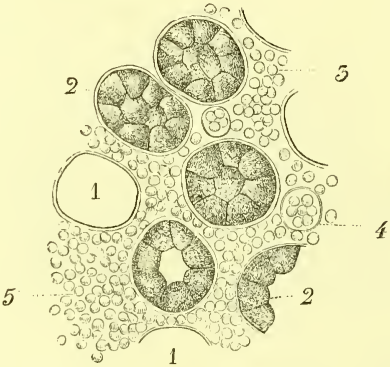

FIG. 140.—TRANSVERSE SECTION OF THE KIDNEY IN LEUCOCYTHEMIA.

1. Lumen of an uriniferous tube the epithelial cells of which have fallen out. 2. Tube, the lumen of which is filled with granular epithelial cells. 3. Capillary seen lengthwise filled with white corpuscles. 4. Transverse section of a capillary. 5. Mass of white corpuscles proceeding from the rupture of capillaries. Magnified 350 diameters.

Lymphadenomata of the small and large intestine greatly resemble those of the stomach; between the largest of them there is no apparent difference; but in the intestine small accuminated tumours are found, much resembling the hypertrophied follicles of typhoid fever, ulcerated and depressed at the centre. It might be thought that there was here simply hypertrophy of a solitary follicle, but it is nothing of the kind; on examining sections of these little tumours under the microscope, the glands of Lieberkühn are seen to be separated by a newly formed reticulated tissue, and below them the same tissue replaces the corium of the mucous membrane. Bœttcher has spoken of adenoid tumours of the *lung*, but he does not describe the structure of the new tissue in a precise manner, and according to the facts observed by ourselves we are inclined to think that the appearances are due to extravasation of white corpuscles, and to foci of catarrhal pneumonia rather than to new growths of adenoid tissue. It is nevertheless possible that adenoid tumours may be produced in the lungs. In *bone*, lymphadenoma is characterised by a well-developed retiform tissue the meshes of which are filled with lymph cells (fig. 144). Lymphadenomata are common in all the organs we

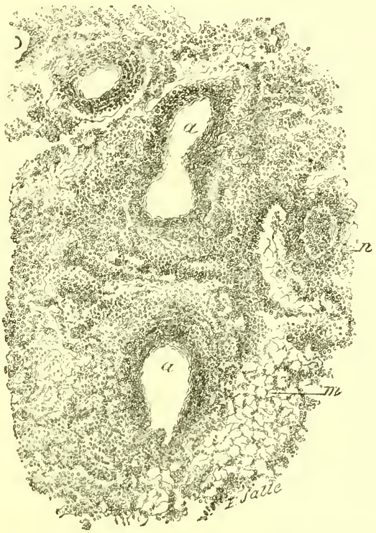

FIG. 141.—TRANSVERSE SECTION OF A LYMPHADENOMA OF THE TESTICLE.

a, lumen of the seminal tubes (magnified 40 diameters). All the tissue belonging to the walls of these tubes and the connective tissue of the testicle are transformed into a retiform tissue, as is very clearly shown in fig. 142, drawn with a higher power.

have been considering, but they may also be met with in the testicle, skin, subcutaneous and intermuscular connective tissue, &c.

A singular form of lymphadenia is that which commences in the skin and may remain entirely confined to it. This is **cutaneous lymphadenia,** long called *fungoid mycosis.* This affection is characterised by tumours varying greatly in size, some of which may, at a given moment, be undergoing retrogressive changes, whilst others are stationary or in process of development. They are composed of a new formation of perfect adenoid tissue located in the corium. The new tissue is developed between previously existing bundles of connective tissue which it separates so as to insinuate itself (fig. 143). It is hence easy to

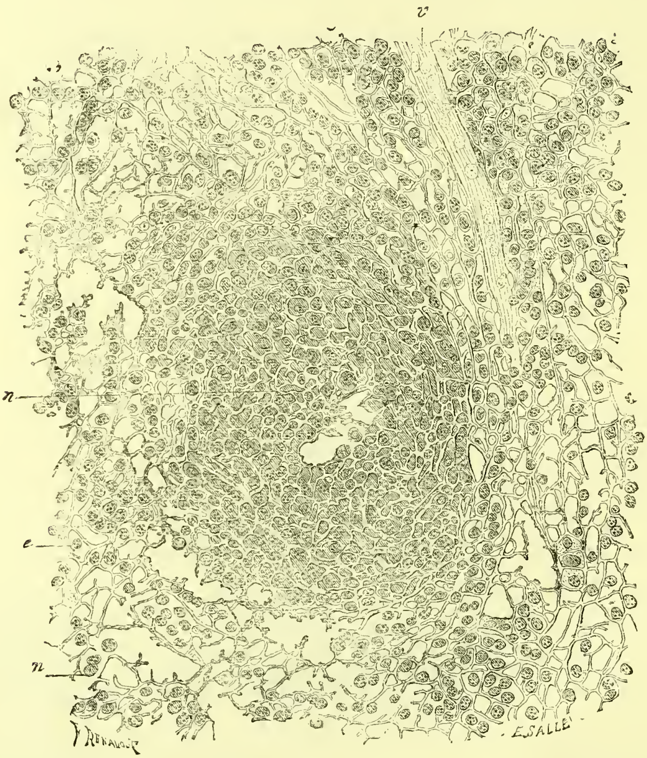

Fig. 142.—Section of a Lymphadenoma of the Testicle, traversing a Seminal Tube.

n, section of the seminal tube, the wall of which is very much thickened and transformed into adenoid tissue; in the very narrow channel, a few free cells are seen; *e*, fibres of the reticulated tissue; *n*, lymph cells. Magnified 300 diameters. (After a preparation by M. Malassez.)

understand how if the neoplasm disappears, the elements of the corium simply return to their primitive relations without a cicatrix being produced. A solitary tumour of cutaneous lymphadenia

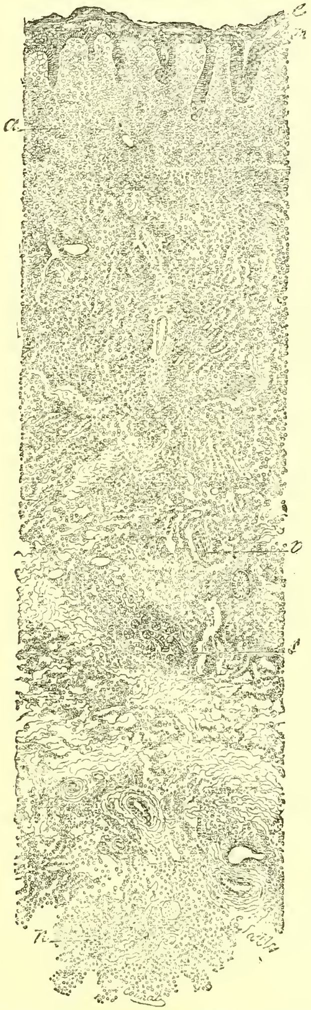

Fig. 143.—Section of Skin affected with Cutaneous Lymphadenia.

l, *m*, epidermal layers, below which are seen the tumefied papillæ. In the tissue of the corium, and in the cellulo-adipose tissue, adenoid tissue is seen, in which the elements of the skin, the sudoriparous glands, *s*, and the blood-vessels, *v*, can be recognised. The thickness of the corium is considerable. Magnified 20 diameters.

has then no positive tendency to persist and to extend. Hence it may appear that after the definitions we have formulated it ought not to be included among tumours; but the exception is only apparent, for the neoplasm, considered as a whole, persists and has even a marked tendency to extend.

The **development of lymphadenoma** can only be well followed in organs where adenoid tissue does not physiologically exist, as in the liver, kidneys, testicles, skin, and bones. The first phase of development is the production of a mass of embryonic tissue from the interstitial connective tissue of the organ, and perhaps also from white blood-corpuscles extravasated from the vessels. Soon, however, trabeculæ of lymphoid tissue are formed, in the meshes of which cells are imprisoned. Such is at least the most natural interpretation of facts observed in tissues of simple structure, as in the marrow of bones for example (fig. 144).

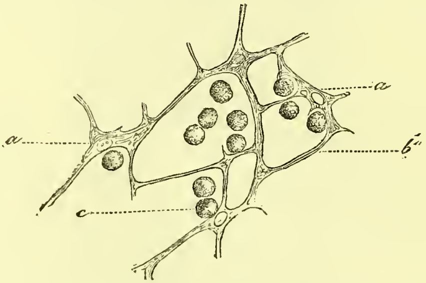

FIG. 144.—ADENOID TISSUE DEVELOPED IN THE OS INNOMINATUM.

a, flat cells applied against the trabeculæ; *b*, fibrils of the developing stroma; *c*, a few cells contained in the meshes of the reticulum. Magnified 500 diameters.

Lymphadenomata are subject to various modifications of their tissue. Diffuse hæmorrhages are often observed, either in the lymphadenomata alone, or at the same time in them and in the organs in which they are located. This occurs particularly in leucocythemia; in which case the extravasations are explained by rupture of the capillaries, consequent on the accumulation of

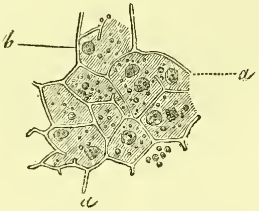

FIG. 145.—ADENOID TISSUE OF LYMPHADENOMA OF BONE UNDERGOING CASEOUS DEGENERATION.

a, filament of atrophied stroma; *b*, lymph corpuscles in a state of caseous degeneration (the tubercle corpuscles of Lebert). Magnified 500 diameters.

white corpuscles within them. The white corpuscles being adhesive and their number considerable, in some cases exceeding that of the red corpuscles, it is easily understood how the circulation may be impeded, and the blood pressure become so great as to cause rupture of the vessels; the effused blood then undergoes the usual retrogressive changes. Sometimes the stagnation of blood in the vessels causes coagulation, and infarcts are then formed (see changes in the vascular system). These infarcts are common in leucocythemia; we do not know if they exist in lymphadenoma. They are characterised by whitish, opaque, caseous spots, in which adenoid tissue is still met with, but both the stroma and lymph cells are atrophied (fig. 145). The blood-vessels are transformed into granular fatty tracts, opaque to transmitted light.

The **diagnosis of lymphadenoma** can only be made in microscopic sections, cut after hardening and from which the cells have been brushed away; the presence of a reticulated stroma is the true characteristic.

The **prognosis** is always very serious. Leukæmia, adenia, and cutaneous lymphadenia are fatal, and the progress of the disease is generally rapid.

IX.—TUMOURS OF THE TYPE OF EPITHELIAL TISSUE.

The most essential characters of physiological epithelial tissue are that the component cells are joined together by an ill-defined substance or cement, and that the tissue is spread out in investing layers containing no blood-vessels. The existence of a substance cementing the cells together, the absence of blood-vessels, and the arrangement of the cells in layers of investment, are the three terms of the definition of epithelial tissues. The tissue may consist of a single layer of cells, or these may be stratified. Stratified epithelium is the most important form to study as regards epithelioma, for here indeed there is an evolution of the cells identical to that met with in epithelial tumours. For example, on the surface of the skin from the papillæ to the superficial epidermis, a series of layers are found, in which the form of the cells varies according to their evolution, and according to the pressure put upon each layer. The cells implanted on the papillæ are cylindrical, and perpendicular to the surface of implantation; their nuclei are large and ovoid, their protoplasm slight in quantity, and they are intimately united to adjacent cells; on their surface they show dentations which are not however so easily seen as in the cells above them. These are larger than the preceding; and polygonal, well-marked filaments hold them together, leaving clear interspaces in which is found a substance less refractive than the filaments themselves. These polygonal cells form a layer, the thickness of which varies according to the region. The next layer is formed of cells slightly flattened towards the surface, and filled with granules, of variable size, which stain with carmine. The nuclei of these cells already look atrophied. This layer of granular cells is called the *stratum granulosum.* To this succeeds the *stratum lucidum* of the epidermis, composed of flattened homogeneous cells of ill-defined limits, and of which the nuclei have already undergone more or less complete atrophy. Above the stratum lucidum is the horny or keratic layer in which the cells, reduced to simple dried laminæ, form a collection of strata. Thus the deeply placed cells of the Malpighian layer become by gradual evolution the polygonal cells of the rete mucosum, the granular cells of the stratum granulosum, the flattened cells of the stratum lucidum and the epidermic scales of the keratic layer. This example shows what variations the same epithelial cell may undergo, and it would be easy to cite numerous other examples. Thus, a polypus developed in the cervix of the uterus, and covered in the first instance by cylindrical cells, shows in its vaginal portion, at the end of a certain time, pavement epithelial cells. If, in a later stage, this polypus were to project at the vulva, all that part of the epithelium in contact with the air would be covered by a layer of dried scales or keratic cells. This transformation of soft into horny epithelium may be traced in a great number of other instances. Thus in certain cases of long-established ectropion, the mucous membrane of the conjunctiva is partially covered by a horny layer similar to that of epidermis. The origin of epithelium in the embryo has already been described (p. 35), and we have seen that the distinctions made by His between epithelium and endothelium cannot be accepted with absolute confidence. The opinion of Thiersch that all epithelium is produced from previously existing epithelial cells seems to us to be contradicted by the formation of epithelium on the surface of granulations and in fistulæ, it being very probable that there the epithelial elements spring from embryonic tissue. The history of cancroid shows very positively that epithelial cells are developed in parts normally deprived of them, for example, in the marrow of the bones, the lymphatic glands, and the muscles. These facts cannot be explained by the continuity of the tumour with an epithelial tissue, for nodules of cancroid may be produced by a process of discontinuous development. Thus, while recognising that the development of epithelial from embryonic tissue is difficult to observe, and can only be followed in very limited spaces, we do not admit Thiersch's theory as absolute.

In epithelial tumours the arrangement of the tissue varies greatly and constitutes many distinct kinds or classes of tumours.

I. **Epithelioma properly so called** in which the new epithelial tissue is arranged in small or large masses without presenting any definite form, such as that of glands or the covering of papillæ.

II. **Papilloma,** in which the epithelial tissue covers papillæ.

III. **Adenoma,** in which the epithelium affects the arrangement observed in glands.

IV. **Cysts,** in which the epithelium lines a cystic cavity.

I. Epithelioma.

Definition and classification of epithelioma.—Epithelioma is also designated by the name of *cancroid*, *epithelial cancer*, or even *epithelial carcinoma*, by German authors, a name introducing a regrettable confusion. The *polyadenoma* and *heteradenic tumour* of many French authors is nothing more than certain varieties of epithelioma. Sometimes the cells of epithelioma are arranged in stratified layers, as in the buccal mucous membrane or the skin, sometimes they are cylindrical and only form a single layer. In the first case the epithelioma is pavement, and in the second it is epithelioma of cylindrical cells.

A. **Pavement epithelioma** itself contains many species.

1. **Lobulated epithelioma.**—In this species the epithelial masses form irregular lobules, in which from the periphery to the centre, stratified layers of epithelium are recognised undergoing an evolution similar to that of cutaneous epithelium; that is to say, that the cells, cylindrical and small at the edge of the lobules, become tesselated, then horny or colloid as they approach the centre of the lobule.

2. **Pearly epithelioma.**—The epidermic evolution is less marked, and all the cells of the lobule may become horny.

3. **Tubular epithelioma.**—The fibrous tissue forming the

stroma of the tumour is grooved by cavities in the form of tubes filled with pavement cells showing no epidermal evolution.

B. **Cylindrical-celled epithelioma** contains but one species. We will proceed now to describe the four kinds of epithelioma properly so called.

1. **Lobulated pavement epithelioma.**—This species has served as the type for the classic description of cancroid. It is generally observed in the skin and those mucous membranes presenting pavement epithelium. With the naked eye it has a granular appearance. On section the surface shows a grey or rose-tinted tissue, in which opaque or translucent spots and fibrous tracts are distinctly seen. The tumour is of unequal consistence, very friable at certain points, dense at others. Generally it can be easily broken up, which fact led Cruveilhier to give it the name of *friable cancer*. On scraping the divided surface with a scalpel, an opaque substance is obtained not miscible with water, while carcinoma juice is miscible with water and gives it a milky appearance. In these scrapings cells of various form are found, some resembling the epithelial scales of the mouth, others showing one or more processes, fusiform when seen sideways and flat when their superficies is presented. Sometimes spherical cells are found distended by a colloid vesicle, which contracts on the addition of acetic acid (Förster). The dentate cells of the mucous layer are rarely isolated by scraping, which is easily explained by the adhesion of these cells together. By scraping, balls are however often found composed of epidermic cells arranged in concentric layers like the leaves of an onion (*c*, *b*, fig. 147); these are epidermic spheres or bird's-nest bodies. In the centre of these bodies there are sometimes colloid cells; cells may also here be found containing a more or less considerable number of nuclei, indicating that there is great formative activity. Thus we see that scrapings

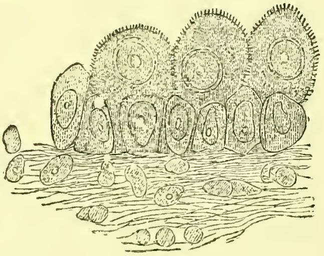

FIG. 146.—DENTATE EPITHELIAL CELLS OF CANCROID.
Magnified 450 diameters.

from the surface of a divided tumour may furnish some indications of the tissue composing it, but are useless for complete definition. To obtain more precise information the tissue of the tumour must be studied in sections cut in different planes. If the section is made perpendicular to the surface of the tumour, lobules are seen formed of epithelium and united together by epithelial tracts. In sections cut parallel to the surface of the tumour, isolated lobules are seen divided transversely.

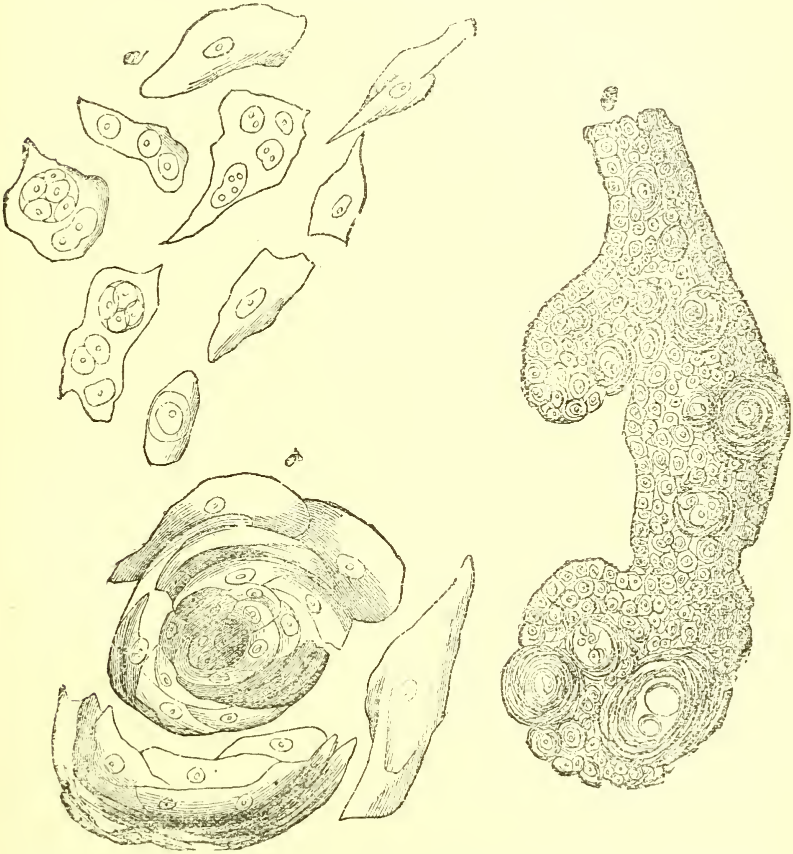

Fig. 147.—Elements of Lobulated Pavement Epithelioma of the Lip.

a, isolated cells showing a multiplication of their nuclei; *b*, epithelial bud with epidermic bird's-nest bodies; *c*, crushed bird's-nest body. Magnified 400 diameters.

The lobules are formed of epithelium similar to that of the epidermis. At the periphery, the cells are cylindrical and implanted perpendicularly on the wall of the cavity; from the periphery towards the centre an epidermic evolution is observed similar to that of the epithelium of the skin ; that is to say there is first a layer of dentate cells, then of flat and horny cells which become dessicated and nested in one another filling up the centre of the cavity and forming what is called a bird's-nest body. The mode of formation of these epidermic bird's nests is easy to understand, on the datum of epidermic evolution from the periphery to the centre of a spherical cavity. The lobules are separated from one another by stroma, generally formed of connective tissue, which supports the arteries, veins, and capillaries. These vessels never penetrate into the substance of the epithelial masses.

The varieties of lobulated pavement epithelioma are in relation with histological modifications of the stroma and nutritive changes in the cells. The stroma may be composed of (*a*) embryonic tissue with numerous blood-vessels; (*b*) mucoid connective tissue; (*c*) adult or fasciculated connective tissue; (*d*) all these varieties of tissue united. The stroma is more or less dense, and sometimes in the same tumour all the varieties intermediate between embryonic and fibrous tissue may be observed. In epithelioma in a state of active growth the embryonic stroma may vegetate on the free surface of the tumour in the form of villi. The epithelioma is then said to be villous.

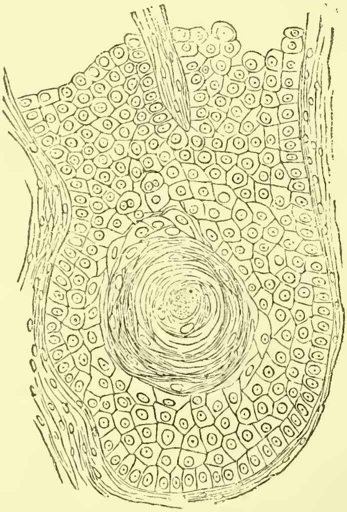

Fig. 148.—Section of Lobulated Pavement Epithelioma.
Magnified 250 diameters.

The varieties of epithelioma related to nutritive modifications of the epithelial cells are two in number, the *colloid* and *keratic.* In the colloid variety the epithelial cells undergo changes similar to those observed in the epidermis, when the epidermal cells, instead of drying, become colloid as the result of irritation. At the commencement of the morbid change the nucleoli of the dentate cells, in consequence of excessive supply of nutritive fluids, become vesicular. The nucleus is itself finally distended by the vesicular nucleolus. This change is observed in the cells of lobulated epithelioma as well as in the epidermal layer of the skin. Soon the cells themselves become vesicular and filled with colloid matter; they may then communicate with one another and form an areolar system, the trabeculæ of which are formed of flat epithelial cells. These elementary lesions, observed in vesicles and pustules of the skin, are often also seen in epithelioma, but here the change more commonly consists in the formation of a droplet of colloid matter. This may be developed in the nucleus replacing it, or may appear round the nucleus; often also it is seen in the protoplasm of the cell, the nucleus being pushed towards the periphery. Colloid and horny change in the cells of epithelioma may sometimes exist in the same tumour, but they more often exist singly, the epithelioma being decidedly colloid or horny.

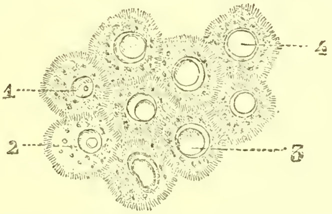

FIG. 149.—EPIDERMAL DENTATE CELLS, THE NUCLEI OF WHICH HAVE BECOME VESICULAR BY REASON OF DILATATION OF THE NUCLEOLUS.

1. Normal nucleus and nucleolus. 2. Dilated nucleolus. 3 and 4. The same change at a more advanced stage.

Lobulated epithelioma is subject to ulceration, which is caused by disintegration of the epithelial cells or by gangrene consequent on obliteration of the blood-vessels. In the first case, the constituent cells of the lobules become detached from one another by softening of their cementing substance, and form a soft mass, which can be squeezed out from the tumour by lateral pressure. At the same time the connective tissue, which separates the epithelial islets, is the seat of an abundant new formation of cells, in which process diapedesis of white corpuscles probably plays an important part. This new formation is accompanied, on the surface of the epithelioma, by a growth of connective tissue which may be so active as to produce granulations. These granulations are generally lined by a layer of pavement epithelial cells, and the surface of the morbid mass then becomes papillary. A partial or total gangrene of the tumour is caused when the epithelial lobules become enlarged, and press upon and obliterate the neighbouring blood-vessels. Sometimes the arterioles and veins contained in a tumour are obliterated by the inflammatory swelling of their internal membrane, from which result more or less extensive modifications of the tumour. The surface of epithelioma at the neck of the uterus is often ulcerated and gangrenous; for to the above-mentioned causes of gangrene is added the irritating action of vaginal mucus.

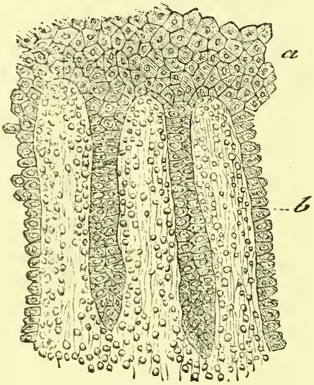

FIG. 150.—SURFACE OF AN EPITHELIOMA WHICH HAS BECOME PAPILLARY.

epithelium; *b*, papillæ; section made according to their longitudinal diameter.

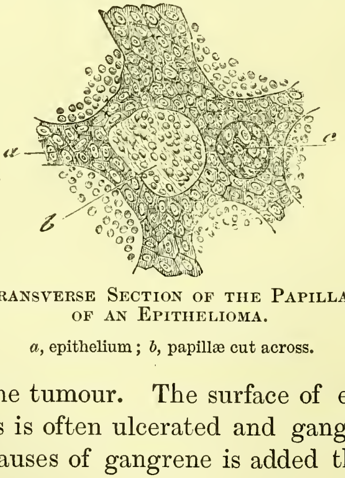

FIG. 151.—TRANSVERSE SECTION OF THE PAPILLARY SURFACE OF AN EPITHELIOMA.

a, epithelium; *b*, papillæ cut across.

Development of lobulated epithelioma.—Lobulated epithelioma develops at the expense of the investing epithelium of the skin and mucous membrane, or from newly formed embryonic tissue in its neighbourhood. Rindfleisch maintains that new epithelial tissue is not developed by proliferation of pre-existing epithelial cells, but by the apposition of such cells. We recognise the correctness of this view in many cases, and think it can be explained by a kind of 'catalytic action.' We see in it a fact analogous to that observed when embryonic tissue, of whatever source, is converted into bone in the neighbourhood of bone. Lobulated epithelioma is however most usually developed by an extension of the rete mucosum situated in the inter-papillary spaces of the skin. The cul-de-sac between the papillæ enlarges, and the epithelium extends by throwing out buds composed of newly formed embryonic tissue, which penetrate deep into the corium. These buds are constricted from place to place, which gives them a lobulated appearance. Epitheloid buds often spring laterally from older buds, and they may even become separated from one another. Epithelial masses may also spring from the hair follicles. The epithelial cells of the external sheath of the hair follicle proliferate, the hair falls out, the limiting membrane of the follicle disappears, the neighbouring dermo-papillary tissue penetrates by epithelial buds, and the rest of the process is as in the preceding case. In the sebaceous glands, which normally possess only one or two peripheral layers of pavement epithelium, the centre of the saccule being filled with fat cells, the pavement cells of the periphery are seen, at the commencement of epithelioma, to increase in number and to push the fat cells to the centre whence they are soon extruded (fig. 152). The limiting membrane of the gland disappears. In this way sebaceous glands are transformed into lobules of epithelioma. The peripheral connective tissue is soon also transformed into embryonic tissue. The phenomena which take place in the sudoriparous glands are still more interesting. These tubular glands, convoluted at their deep extremity in the form of glomeruli, are lined with a simple layer of pavement epithelial cells within the limiting membrane. In epithelioma an accumulation of epithelial cells is first observed in the interior of the gland, so as to fill up and distend the primitively hollow tube. These solid cylinders of epithelium send out epithelial buds into the adjacent embryonic tissue which unite together to form a network; they are all formed of small pavement cells. It is by the ulterior metamorphoses of these epithelial cylinders that islets of lobulated epithelioma are produced. In fact, a certain number of these cylinders enlarge, the cells at the periphery remaining small and implanted on the wall, but as the centre of the enlarged tube is approached the cells become larger, undergo horny or mucoid change, and concur in the formation of bird's-nest bodies. All the phases of this evolution may be followed in the same tumour. The lobules become finally isolated as in the previous examples.

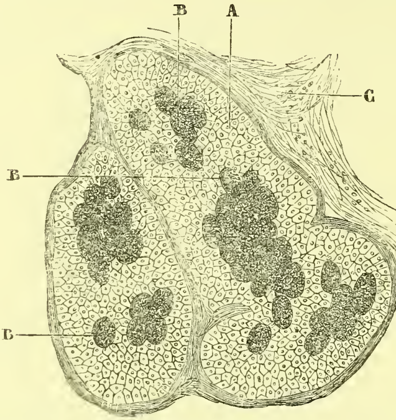

FIG. 152.—PROLIFERATION OF THE EPITHELIAL CELLS OF SEBACEOUS GLANDS IN A CASE OF EPITHELIOMA.

A, epithelial cells in a state of growth; B, sebaceous cells filled with fat; C, neighbouring connective tissue. Magnified 150 diameters.

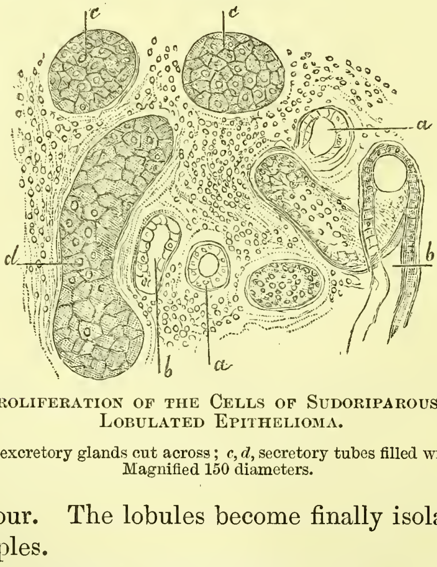

FIG. 153.—PROLIFERATION OF THE CELLS OF SUDORIPAROUS GLANDS IN LOBULATED EPITHELIOMA.

a, *b*, sudoriparous excretory glands cut across; *c*, *d*, secretory tubes filled with epithelial cells. Magnified 150 diameters.

Growth and extension of epithelioma.—Whatever may be its mode of origin lobulated epithelioma continues to extend by proliferation of its own proper mass, the lobules becoming larger; or else new centres of epithelioma similar to the primitive tumour are formed in the neighbourhood. The papillæ, hair follicles, and glands, adjacent to cutaneous epithelioma, show the same phenomena as those described in the primary development of the tumour. If in the immediate neighbourhood of epithelioma there is striated muscular tissue, as in the lip or tongue, changes similar to inflammation first take place. The muscular fasciculi are separated by connective tissue rich in cells, or by embryonic tissue, and the nuclei of the sarcolemma enlarge and multiply.

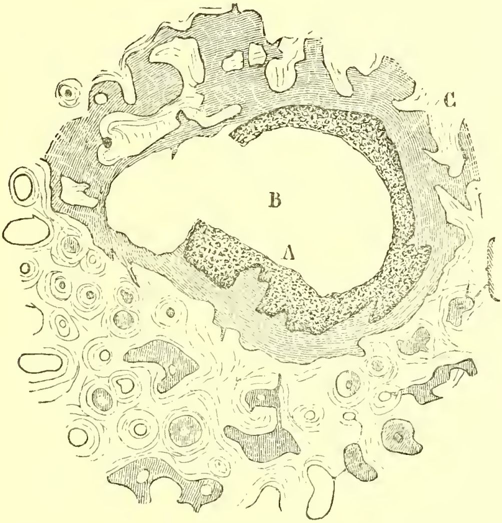

FIG. 154.—SECTION OF A LOBULE OF EPITHELIOMA LOCATED IN THE MIDST OF BONE.

Some of the epithelial cells of the lobule have fallen out in making the preparation, leaving the empty space, B. At A, they have remained. C, osseous lamellæ. Magnified 20 diameters.

In these cases the presence of large nuclei with voluminous and brilliant nucleoli having been observed under the sarcolemma, some authors have supposed that the muscular tissue was infiltrated with epithelial nuclei; but this opinion, based on the form of the nuclei and nucleoli which was erroneously considered to be characteristic of epithelioma, must be rejected. The muscular fasciculi atrophy, in consequence of the pressure of the inflamed connective tissue or of the lobules of epithelioma developed in it. They still, however, preserve their cylindrical form, or, constricted at certain points they become moniliform, a change observed in other tumours of the muscles (fig. 79, *a*). The fasciculi contained in the morbid mass almost always show fatty infiltration or vitreous degeneration. In muscle, epithelioma extends by means of the embryonic mass which has taken the place of the muscular fasciculi and insinuated itself often for a long distance between them. In extending an epithelioma may approach superficially situated bone, such as the maxillæ, the bones of the nose, the os frontis, the sternum, &c.; in which case the osseous tissue near the neoplasm shows lesions analogous to those of inflammation. Embryonic medulla is produced, the osseous lamellæ are destroyed, the medullary cavities enlarged, and here again, it is in the midst of embryonic tissue that the epithelial buds are pushed out. A lobule of epithelioma located in an enlarged medullary cavity is

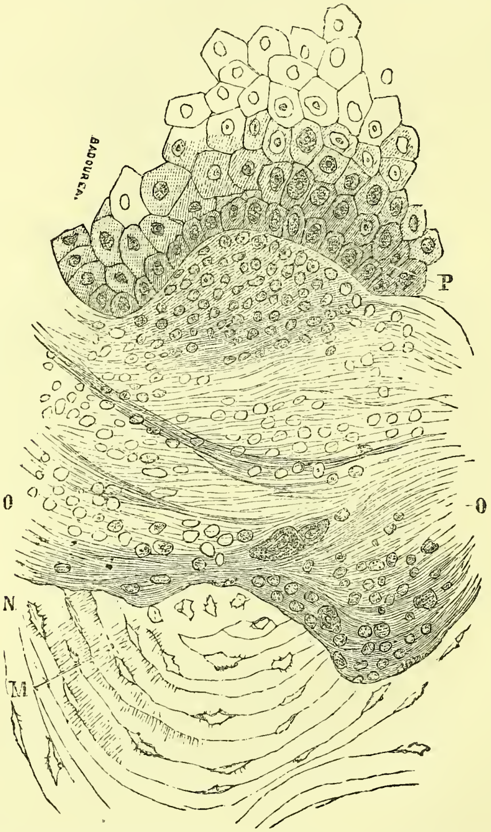

FIG. 155.—A PART OF THE PRECEDING FIGURE MAGNIFIED 300 DIAMETERS.

P, epithelial cells of the islet of epithelioma represented at A in the preceding figure, O, tissue composed of fibrous medulla; M, osseous lamellæ notched; N, bone corpuscles.

surrounded by embryonic tissue, which is in contact with irregularly festooned osseous lamellæ (see figs. 154 and 155).

Generalisation of epithelioma.—Epithelioma is frequently generalised in the form of nodules which originate far from the primary tumour, either in the nearest lymphatic glands or in the internal viscera, the lungs, liver, kidneys, and even the heart. It should be stated however that secondary growths in the viscera are rare, and that their histological development has not been hitherto well studied.

The **prognosis of lobulated epithelioma** differs greatly according to the structure of the tumour and its seat. The most serious cases are those in which the stroma is entirely embryonic, and the connective tissue at the periphery of the tumour in an embryonic state; for this signifies that the epithelial mass is spreading rapidly. Epithelioma develops most rapidly in those parts of the body most plentifully supplied with lymphatic vessels, and where the circulation of the blood is active, and also in parts exposed to causes of irritation. For example, the moist mucous orifices, subject to movements or contusions, the lips, tongue, eyelids, cervix of the uterus, &c., are the seat of epitheliomata as rapid in growth and as surely fatal as the most malignant carcinomata; and yet in structure such tumours are identical with epitheliomata of the skin, nose, and cheek, which may remain quiescent for ten, fifteen, or twenty years without increasing in size or causing serious accidents. The epitheliomata which extend slowly are generally superficial and they often show a cicatrix at the centre while the tumour is spreading at the periphery. After being long stationary they may however rapidly increase and invade the deeper structures. This shows that the malignity of a tumour is often less related to its histological type than to its seat and mode of development.

II. Pearly pavement epithelioma.—This tumour was called *cholesteatoma* by J. Müller, who confounded many different tumours under the same name. It has a certain analogy to lobulated epithelioma, as it is itself lobulated and often encysted. Its surface on section is dry, opaque, whitish, slightly luminous like cholesterin; but this is only a coarse resemblance, there are in fact but few cholesterin crystals present in these tumours, not more than are met with in the softened parts of lobulated cancroid, and the shining appearance is due to dessicated epidermic lamels. On scraping, small beads are obtained visible to the naked eye, regularly round and formed of many lobes united by enveloping concentric layers. On microscopical examination, these little granules are seen to resemble the spherules of the choroid plexus or of angiolithic sarcoma; but they contain no calcareous salts. When stained with carmine, attached epidermic lamels containing atrophied nuclei become apparent in their external layer. Beside these epidermic pearls, isolated horny cells may be observed. Sometimes also spangles of cholesterin are obtained by scraping. In delicate sections cut from a fresh specimen, or one which has been preserved in a ·2 per 100 solution of chromic acid, the tissue is seen to be characterised by lobules resembling those of lobulated epithelioma; but on attentively examining these lobules it is seen that their epidermic evolution is stationary. Instead of the stratified layers of cylindrical and pavement epithelium, which are found at the periphery of the lobules of ordinary lobulated epithelioma, there is here but a single layer of flat cells the nuclei of which are atrophied. The pearls are sometimes completely separated from one another, sometimes united by delicate pedicles, themselves formed of epidermic cells. Between the lobules there is a dense connective tissue containing no blood-vessels (Förster). These tumours are very rare.[1] They are quite benign, and remain in an almost mummified condition as foreign bodies, causing no accidents. As they are fully developed and have been long in a stationary condition at the time of their removal, their histological development is unknown. But their resemblance in seat and structure to lobulated epithelioma allows of the hypothesis of a similar development. The cause of their benign nature and of their mummification is likewise unknown.

III. **Tubular epithelioma.**—This tumour has been called *cylindroma* by Billroth, *polyadenoma* by Broca, and under the name of *heteradenic tumour* Robin has described both lobulated and tubular carcinoma and epithelioma, and many other ill-defined tumours. Epithelioma developed from the sudoriparous glands, so well described by Virchow, partly belongs to these species.

Definition.—Tubular epithelioma may be defined as a tumour composed of tracts or cylinders of pavement epithelium undergoing no epidermic evolution, which anastomose together and are located in a stroma formed of embryonic, mucous, or fibrous tissue. The first stage in the development of lobulated epithelioma from the sudoriparous glands (see p. 263)—when the tubes filled with pavement cells are converted into solid cylinders anastomosing together—is the final stage in the development of tubular epithelioma. But still all tubular epitheliomata are not cancroids which have commenced in the sudoriparous glands and been arrested in the first stage of development; for tubular epithelioma may be present in organs which have no sweat glands, as in the uterus, and even where there are no epithelial glands at all as in the lymphatic ganglia.

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[1] Though for many years we have collected and examined a great number of tumours for the hospitals of Paris and the Anatomical Society, we have met with but three examples of these tumours.

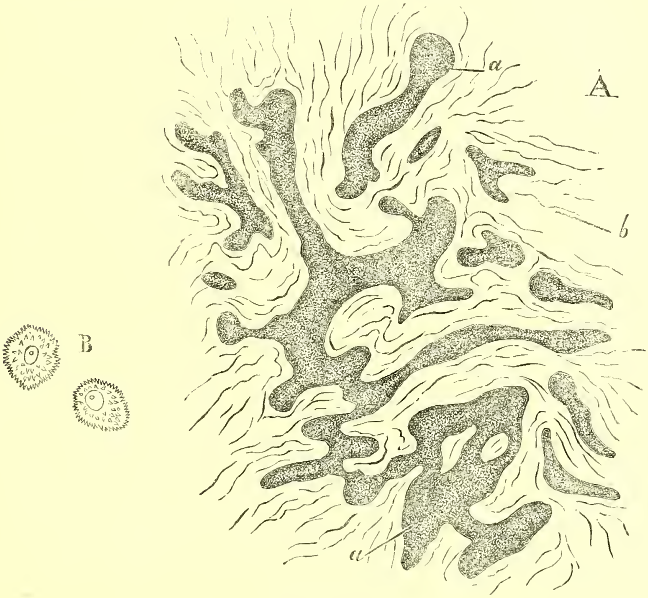

Fig. 156.

A, Section of tubular epithelioma. *a*, solid cylinders composed of pavement epithelium; *b*, stroma hollowed by tubes which lodge the cylinders. Magnified 20 diameters. B. Epithelial cells of the same tumour isolated and showing the dentations by which they are united. Magnified 400 diameters.

Description of tubular epithelioma.—The tumour is regular, spherical, or ovoid in form; on section it shows a greyish tissue resembling that of a gland or sarcoma. The diagnosis is impossible with the naked eye. No juice is yielded on pressure. On examining scrapings under the microscope some notions may be obtained as regards the structure of the tumour under examination. Segments of cylinders composed of pavement epithelium are found; they are sometimes branching, their edges are regular, generally parallel, and their extremities are limited by sinuous, irregular borders, the result of fracture. The cells composing them are small, equal in size, with ill-defined dentate borders, so that with a low magnifying power their edges are not clearly distinguished, but well-marked nuclei are seen in the midst of a granular substance. It is owing to the dentate borders and the intimate union of the cells that they cannot be isolated in the fresh state. The dentate cells can, however, be isolated twenty-four or thirty-six hours after the removal of the tumour, owing to cadaveric decomposition which softens the cementing substance (*b*, fig. 156). Besides these cells fusiform cells, free nuclei, cells and even flakes of connective tissue may be found. But the various elements obtained by scraping are not truly characteristic of this species of epithelioma; for at the commencement of carcinoma of a gland, we may find in the scrapings fragments of epithelium in the form of solid cylinders, produced by a new formation of epithelium in the glandular ducts of the invaded region.

In delicate sections made after hardening in alcohol or in a ·2 per 100 solution of chromic acid, cylinders composed of pavement epithelium are seen anastomosing together, and arranged in a stroma of variable composition. The epithelial cells are dentate, their borders ill defined unless the section is extremely delicate. The stroma is generally fibrous and very dense, but sometimes it is mucoid. In such a mucoid tissue surrounded on all sides by epithelial tracts, the connective-tissue cells are generally degenerated and destroyed, and from them are formed little cavities filled with mucus. It might be thought that these cystic cavities were caused by degeneration of the epithelium, while they on the contrary result from alteration of the stroma. Rindfleisch has given to tumours containing them the name of *cystic epithelioma*. The pavement cells of all tubular epithelioma may undergo colloid degeneration; when colloid spherules having a diameter of 20 μ to 50 μ may be seen here and there, in the epithelial tracts. Sometimes also at certain spots these tumours may show an epidermic evolution. Lobules are then seen with horny cells at the centre, an arrangement which connects tubular epithelioma with lobulated epithelioma proper.

Seat and development of tubular epithelioma.—When located in the *skin*, it develops from the sudoriparous glands. This mode of origin was long ago observed by Verneuil; it is here developed in exactly the same manner as lobulated epithelioma (p. 263). Being seated in the deep layers of the skin tubular epithelioma ulcerates more slowly than lobulated epithelioma. It is also produced by modifications of tubular glands in the cervix uteri, and the maxillary sinus, and even from acinous glands, as may be observed in the velum palati. Among the numerous tumours of the mamma described formerly under the name of carcinoma, some may be observed corresponding in every detail to the description of tubular epithelioma. Tubular epithelioma is distinguished from carcinoma of the mamma by the fact, that in carcinoma the cells are not firmly united together so as to form masses or cylinders which can be detached by scraping. Exception must, however, be made in carcinoma of the breast, for the epithelial cylinders which are developed in the galactophorous ducts of large and medium calibre, and which result from the proliferation and accumulation of epithelial cells in their lumen. Such epithelial cylinders may be met with in all tumours of the breast, whatever may be their nature; they result from secondary irritation of the glactophorous ducts caused by the development of the tumour. By obliterating the glandular ducts the formation of cysts is frequently brought about; the wall of these cysts is sometimes regular, sometimes covered by growths formed of the morbid tissue. Hence every tumour of the breast has the property of producing certain morbid forms which are common to all. An exhaustive histological examination is always necessary to determine the nature of a tumour of this organ. Many tubular epithe-

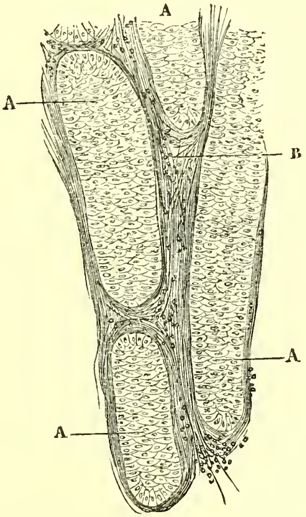

Fig. 157.—Transverse Section of a Tubular Epithelioma.

A, epithelial cylinders divided obliquely; B, fibrous stroma.

liomata, having reached a certain stage of development, remain stationary. Sometimes they continue to extend, in which case the epithelial cylinders terminate in *culs-de-sac* in the midst of an embryonic tissue. Growth then takes place by simple extension, or by successive metamorphoses of neighbouring embryonic cells.

Prognosis of tubular epithelioma.—When located in the skin (*partial sebaceous acne*) it is less serious than lobulated epithelioma, a fact on which Verneuil has rightly insisted. But this benignity must not be understood in too absolute a sense, for tubular epithelioma often relapses after removal. It is often propagated, as we have been able to verify, to the lymphatic glands in which a tissue is formed similar to that of the primary tumour. It is also sometimes transformed into lobulated epithelioma. Among tumours formerly regarded as cancerous, they are the slowest in development. Sometimes after destroying all the glandular elements of a part of a skin, the centre of the morbid mass may cicatrise whilst the periphery continues to extend—in a word, they extend in a similar manner to certain ulcerating chancres. When situated in the neck of the uterus, the prognosis is quite as serious as that of carcinomatous and other epithelial tumours in the same region. Tubular epithelioma primarily developed in the

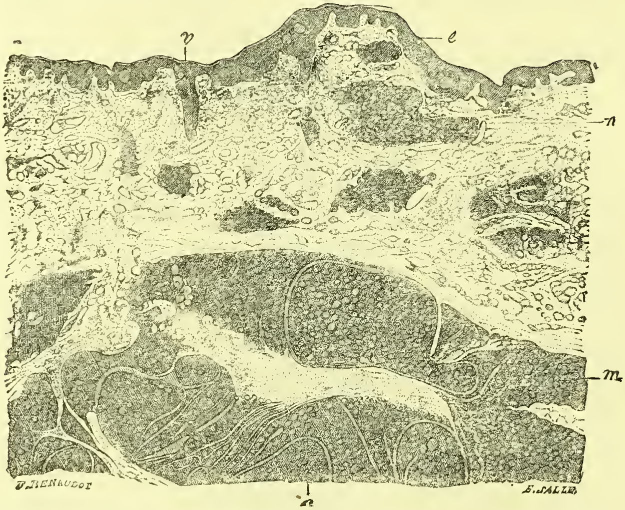

FIG. 158.—SECTION OF AN EPITHELIOMA CONTAINING OVOID BODIES.

This drawing represents a section of the skin and the subjacent tissue magnified 20 diameters. *e*, epidermic layers; *m*, *c*, epithelial tracts and islets located in the midst of a subcutaneous fibrous tissue. This drawing and the following one are from a tumour examined by M. Malassez.

maxillary sinus, a rather common situation, spreads rapidly and is extremely serious.

With tubular epithelioma we must include certain tumours described by Robin, Förster, &c., which present a peculiar arrangement. They are formed of epithelial cylinders and lobules seated in the midst of fibrous tissue (figs. 158 and 159), in the centre of which are found here and there refractive bodies (*c*, fig. 159) united together by anhistic processes. In the interior of these bodies stellate cells are often observed. According to Förster these tumours are epitheliomata; Robin looks upon them as heteradenic tumours. They are very rare, and are, in fact, tubular epitheliomata with mucous connective-tissue growths in the midst of the epithelial mass. The ovoid bodies correspond to buds of mucous connective tissue, and in the pedicle, which unites them to the stroma of the tumour, blood-vessels are often found.

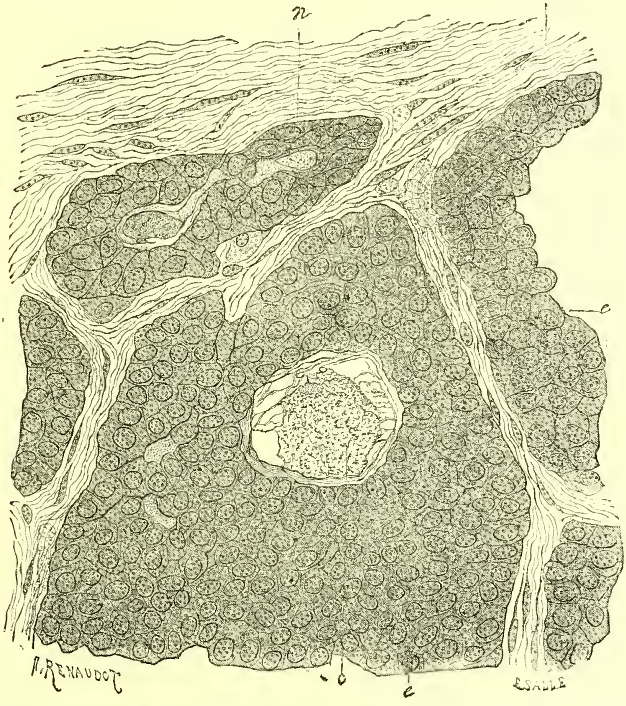

FIG. 159.—SECTION OF THE SAME EPITHELIAL TUMOUR WITH THE OVOID BODIES AS THE PRECEDING, BUT MAGNIFIED 250 DIAMETERS.

n, section of an epithelial tube in the midst of which is a little ovoid body; *e*, a larger epithelial lobule, in the centre of which is a mucous ovoid body, *c*.

IV. **Cylindrical-celled epithelioma.**—This peculiar species of epithelioma, discovered by Bidder, has been well described by Förster and Virchow, and we have ourselves examined and published a great number of cases. It was formerly confounded with encephaloid and colloid carcinoma. It is characterised by tubular or irregularly formed cavities, lined with one or more layers of cylindrical epithelial cells, located in a fibrous, embryonic, or mucous stroma. The cylindrical cells are similar to those which line certain mucous or glandular cavities, and are always inserted perpendicularly on the wall they cover. The naked eye appearances of these tumours vary. In the stomach and intestine they are like nummular prominences, varying both in number and size, generally ulcerated at the centre. When, as is frequently the case, they are propagated to the liver and other organs, they show the same arrangement, dissemination, and naked eye appearances as encephaloid carcinoma. In some cases whitish tracts are seen in section. These tumours have generally an abundance of milky juice, so that this character, taken in connection with their usual softness, might cause them at first sight to be mistaken for encephaloid carcinomata. The softness and juice are, probably in a great measure, due to cadaveric softening. In fact, these tumours, always seated in the internal organs, are never discovered till twenty-four hours after death. Cadaveric softening occurring less rapidly in the winter than in the summer, tumours examined during the cold season yield much less juice.

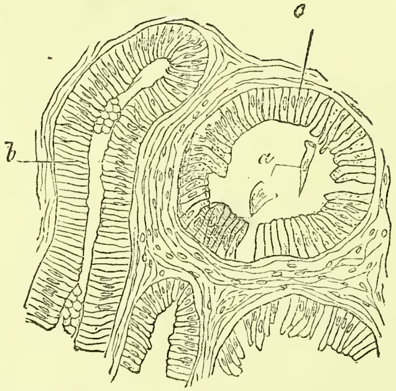

FIG. 160.—TRANSVERSE SECTION OF AN EPITHELIOMA WITH CYLINDRICAL CELLS.

a, tube divided transversely, lined with epithelium, *c*; in the centre are a few free and isolated cylindrical cells; *b*, tube divided longitudinally.

The fluid obtained by scraping is, as in all other epitheliomata, distinctly grumous. The elements contained in the juice are cylindrical cells. On their free surface they often show a double border. Some seen sideways appear like the fusiform elements of sarcoma, others show on their free border a vesicular or caliciform dilatation. They are generally elongated and rod-shaped, measuring 20 μ to 30 μ and even longer; but some are polygonal or more or less irregular. They possess one or more oval nuclei, measuring 10 μ to 15 μ in length, and contain one or more brilliant nucleoli. It is thus seen that there is a certain polymorphia in the cells. Sometimes cylindrical cells may be united by their lateral borders, and show along their free edge a limiting double line. This appearance is so characteristic that it is enough of itself to establish the diagnosis of cylindrical epithelioma.

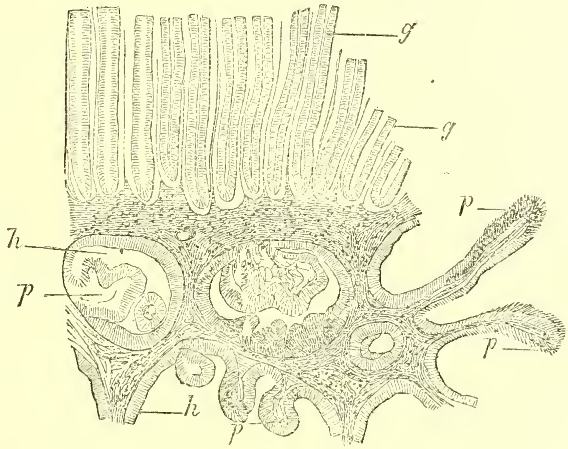

Fig. 161.—Section of a Cylindrical Epithelioma of the Large Intestine.

g, g, layer of hypertrophied glands of Lieberkühn; these glands are destroyed to the right of the drawing, which corresponds to the ulcerated part; *h, h*, cavities lined with cylindrical epithelium. Magnified 40 diameters.

The histological structure of the tumour is ascertained by the examination of hardened preparations: (if the tumour has softened it is as well to immediately use absolute alcohol). In a delicate section it is then seen that the tubular cavities or irregular spaces are lined with cylindrical epithelium. These tubes and spaces, which are sometimes sinuous and have papillæ on their surface, are often distinctly seen to be continuous with neighbouring glands; the latter, hypertrophied, may form a distinct layer on the surface of the tumour if it is situated in the stomach or intestine (see fig. 161). The cells, generally simply arranged, form a regular layer, and are inserted directly into the stroma, without the interposition of any basement membrane (fig. 161). Besides the tubes and irregular cavities thus lined, the surface of the tumour is often covered with papillæ lined with cylindrical epithelium. When development is complete, the stroma is fibrous, but it is often embryonic in tumours of recent date; occasionally it is mucous as in myxoma and composed of round or anastomosing connective-tissue cells. It always contains blood-vessels, which are numerous and similar in structure to those of sarcoma, if the stroma is embryonic. Though usually slight in amount the stroma may predominate and constitute the largest part of the tumour.

Varieties of cylindrical epithelioma may be distinguished according as the stroma predominates or as it is fibrous, embryonic, or mucous. The blood-vessels often dilate, ending in hæmorrhagic ruptures, which is a rather frequent accident in the mucous form. An important and common variety consists in the colloid change of the epithelial cells. They are changed into transparent vesicles, which are successively detached from the wall of the tube and fall into the lumen. A border of cylindrical cells may then be found limiting a cavity filled with colloid substance and the debris of cells. At other times the parietal cells are themselves completely degenerated, in which case the little cavity containing them has no longer any of the characteristics of cylindrical epithelioma. Fatty degeneration is generally associated with colloid change. This form of epithelioma always eventually ulcerates when seated in the mucous membranes. Its superficial destruction is not solely in consequence of the evolution of the morbid tissue, but is also due to the irritating and even destructive action of the fluids with which it is in contact. For example, the gastric juice has a manifest corrosive action on living tissues developed in the stomach, if they are not protected by the physiological epithelium of that organ. On the surface of tumours of the stomach coagula of black blood are often found, broken up in the blood-vessels; this coagulation is due to the action of the gastric juice. The development of cylindrical epithelioma takes [place at the expense of the glands, by a process analogous to that described in pavement epithelioma.

Seat of cylindrical epithelioma.—With the exception of the ovary, this tumour is always found on *mucous membranes lined normally with cylindrical epithelium*, that is to say the mucous membranes of the stomach, small and large intestine, rectum, bile ducts and uterus. Certain soft, polypoid tumours developed in the fundus or cervix of the uterus, and extending into the vagina, and which are difficult to remove on account of their softness, are, in spite of their analogy with certain benign tumours of the uterus, cylindrical epitheliomata and really malignant growths.[1] In the ovary, we have seen non-cystic tumours resembling carcinoma to the naked eye, and which had undergone partly fatty and partly mucoid changes, which were, however, cylindrical epitheliomata. Certain polypi of the nasal fossæ, which with the naked eye cannot be differentiated from other varieties of mucous polypus, correspond histologically to cylindrical epithelioma.

Prognosis.—Secondary growths, the structure of which is identical with that of the primary tumour, are met with particularly in the liver, in consequence of the venous relations of this organ with the intestine. There are also certain well-authenticated observations of the generalisation of cylindrical epithelioma, in the form of nodosities, in the lungs and bones. As they are located in the deep organs it is impossible to differentiate them during life from carcinoma, they have however the same gravity and the same fatal termination.

The anatomical diagnosis is generally easy if attention is paid to the facts unfolded above. Tubular epithelioma must be carefully differentiated from medullary or colloid carcinoma when soft. In secondary and rapidly growing formations of the liver, the centre is softened, and the epithelial cells dissociated and filled with fat granules. The tumour loses its characteristic appearance and becomes riddled with alveoli; so that on brushing away the cells an alveolar stroma is discovered exactly similar to that of carcinoma. The similarity is so great that if the younger peripheral parts were not there to guide the observer, it would be impossible to make the diagnosis. To distinguish cylindrical epithelioma which has undergone colloid change from colloid carcinoma, the most recently formed parts not yet touched by colloid degeneration must be studied with the greatest care.

II. Papilloma.

Papillomata are not regarded by all pathologists as forming a distinct group of tumours. All tumours become papillary under certain conditions; if located on a surface, for example. Thus certain pathologists, Rokitansky among others, describe papilloma as fibroma which has taken on a papillary appearance, and Förster has remarked that papillomata may be described with angiomata, as they nearly always possess as an essential part newly formed blood-vessels. We consider that the definition of papillomata is given by that of the papillæ themselves. Now, it is well known, that papillæ are composed of connective tissue serving to support blood-vessels which terminate in a capillary network or in vascular loops, and that they are covered by an epithelial lining. These normal excrescences, which limit the skin and certain mucous membranes, are sometimes covered by stratified layers of pavement and horny epithelium, sometimes lined by a mucous epithelium. These two normal types serve as the basis for two species of papilloma—**horny papilloma**, and **mucous papilloma.** For a tumour to be called papilloma the body of the papillæ should be composed of connective tissue, and the layers of investing epithelium arranged as upon normal papillæ. The tissue at the base of the papillæ should moreover not be constituted by that of one of the special tumours described in the preceding pages. It is essential in fact that sarcoma, fibroma, carcinoma, and epithelioma, presenting on their surfaces papillary buds,

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[1] *Thesis of Montfumat*, 1867

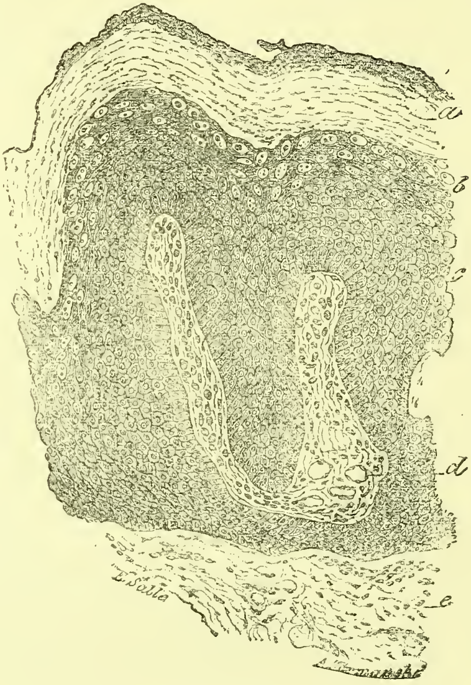

FIG. 162.—HORNY PAPILLOMA OF THE LOWER LIP.

a, horny covering; *b*, granular layer; *c*, rete mucosum; *d*, blood-vessels of the papillæ; *e*, connective tissue. Magnified 100 diameters.

should not be confounded with papilloma. In these cases the tumour should simply take the name of papillary.

I. **Horny papilloma.**—This class contains a number of tumours. Most authors include in it corns, warts, and horns.

Corns seated upon the toes are caused by a constant pressure or irritation. They commence by hypertrophy of the papillæ. The horny layers of the epidermis soon exercise pressure on the papillæ, so as to flatten and drive them down like a nail in the cutis. The latter atrophies, the adipose tissue disappears at the point of pressure, and sometimes a mucous bursa is formed beneath. The papillæ, at first hypertrophied at the base of the corn, soon become depressed instead of projecting in a tumefied manner.

Warts.—In these the papillæ hypertrophy and give origin to secondary papillæ. The covering composed of cells, similar to those of the rete mucosum and epidermis, envelops the entire new papillary mass with a smooth layer; or a certain number of the papillæ are isolated by an epidermic covering proper to each group; from which arrangement the tumour has an unequal, cracked appearance. The connective tissue which surrounds the blood-vessels is found to be less abundant as we pass from the base of the tumour to the superficial secondary papillæ. In a transverse section, each one of the papillæ on the surface of the tumour shows one or more central disks which correspond to the divided vessels. Around these disks there is a slight quantity of connective tissue bounded by layers of epidermis.

Horns may be looked upon as warts the epidermic cells of which are welded together as in the nails. They are observed in different parts of the skin, but particularlly on the face. They are also met with in dermoid cysts. The epidermic cells of which these horns are composed are not desquamated, but are superimposed indefinitely, from which result hard appendages of various length, and formed of imbricated layers of epidermal cells.

Certain **nævi** are also horny papillomata. They are formed of simple or composite papillæ. Viewed full-face the tips of a great number of papillæ are seen, all covered with layers of dried epidermis; on separating the papillæ, between them at their bases, smaller papillæ are seen covered like the larger ones. These congenital tumours are sometimes deeply pigmented.

II. **Mucous papilloma.**—In this form the papillæ are simple or composite. Villous papillomata are also observed, in which the papillæ by their length and tenuity resemble the villi of the mucous membranes. In papillæ there are two parts to study, the papillary body and the epithelial covering. The papillary body has the form of a more or less voluminous bud which gives origin to a varying number of secondary and tertiary buds. Its variable shape depends upon the new formation of vascular loops. It is composed of connective tissue giving support to blood-vessels which terminate in loops at the extremity of the papillæ. The connective tissue is sometimes so slight in quantity that the epithelial covering seems to rest directly on the blood-vessels. In recent and rapidly growing papilloma, for example in certain cauliflower excrescences of the genital organs, the body of the papilla is formed of embryonic connective tissue. The blood-vessels of papilloma are arteries, capillaries, and veins of normal structure. The capillaries are often dilated in a regular or ampullar manner, haemorrhages being caused by their rupture; the blood escapes or remains imprisoned in the body of the papilla, where it undergoes pigmentary change. The vessels of the papilla may throw out buds, and undergo calcareous degeneration. Villous papillæ are generally simple; they sometimes become very long, particularly when compressed laterally against one another. The epithelial covering of papillæ differs according to the pavement or cylindrical form of the cells. In the first case a large number of layers of cells undergo an evolution identical with that of the rete mucosum, or the epithelial lining of the buccal mucous membrane. The cells are plainly seen to be dentate, those at the surface being flattened. Papillomata often have a covering of pavement cells,

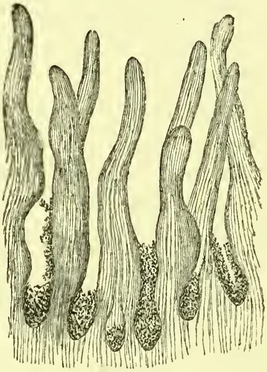

Fig. 163.—Villous Papillæ of new Formation on the Mucous Membrane of the Stomach.
Magnified 60 diameters.

while the mucous membrane whence they spring may be lined with cylindrical cells. When the papillary body is covered with cylindrical epithelium, there is but one layer. The investing cells of papilloma are often vesicular and in a state of colloid degeneration.

The development of mucous papilloma is generally at the expense of the villi or papillæ from which they spring, but they may develop in parts which have no papillæ, as for example in the ventricles of the larynx, or in the stomach. The precise phenomena of these hypertrophies and neoplasms have not been closely followed in papilloma, but the analogy of their structure with that of inflammatory granulations leads to the supposition that their mode of formation is the same. Chronic inflammation is often a cause of the development of papilloma, as may be observed, for example, at the periphery of callous ulcers of the skin and in elephantiasis. Papilloma cannot, however, be considered as identical with inflammatory granulations, for the tendency of the latter is to heal, by the organisation of their elements into cicatricial connective tissue, whilst papilloma tends to persist indefinitely as a tumour. Their termination is thus different, though in their origin they have numerous points of contact. There are nevertheless papillomata, such as the cauliflower excrescences of the genital organs, which may disappear spontaneously or in conse-

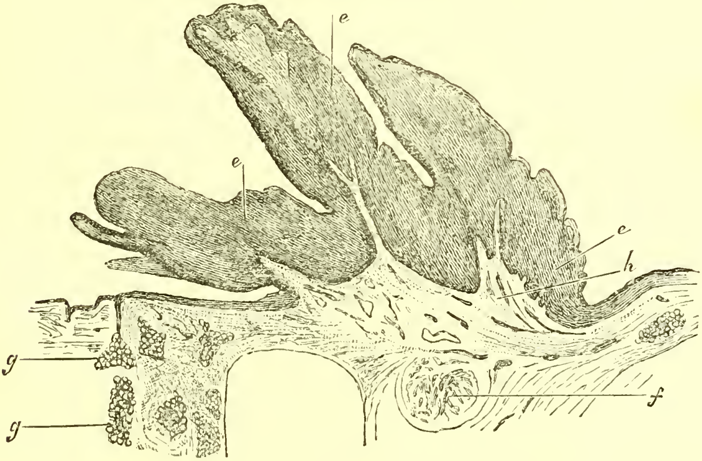

FIG. 164.—PAPILLOMA OF THE LARYNX.

h, base of composite papillæ; *e*, epithelial covering of the papillæ; *g*, normal glands of the mucous membrane; *f*, a gland partly atrophied at the base of the papilloma. Magnified 20 diameters.

quence of local treatment. These may be considered as transitory between tumours properly so called and inflammatory products.

Seat of papilloma.—Mucous papillomata are rather frequently found on the edge of the *tongue*, the *uvula*, and on the mucous membrane of the *larynx*, sometimes on the ventricles of the larynx and on the *vocal cords*. These are generally simple papillomata not complicated with adenoma. They are also rather common in the *gastro-intestinal mucous membrane* (for further details see article on stomach and intestine), where they are often combined with hypertrophy of the glands. On the mucous membrane of the *bladder* and the *urethra* papillomata are developed, composed of long, delicate, villous, and highly vascular papillæ, which bud at the base of the bladder and at the urethral orifice. On both the male and female external genital organs, papillomata commonly called cauliflower growths, spring up from the most varied causes, sometimes they are very small, at others they attain a considerable size. Extirpation is generally necessary, but the irritation consequent on operation may cause recurrence of the growths. Papilloma may be observed in *serous membranes*, particularly in those articular serous cavities which normally possess villi; these may hypertrophy so as to form veritable

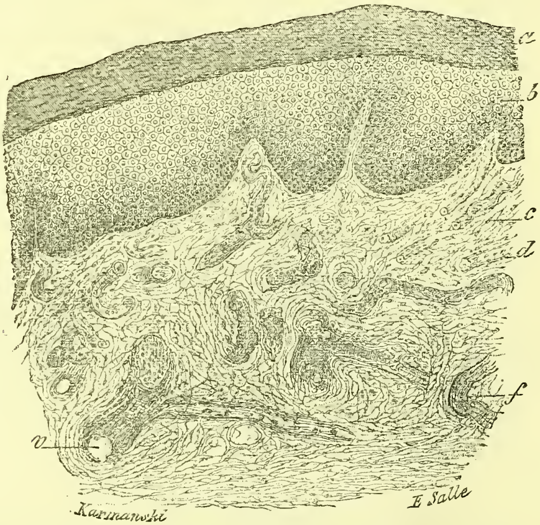

FIG. 165.—PAPILLOMA AT THE URETHRAL ORIFICE.

a, horny layer; *b*, rete mucosum; *c*, connective tissue in which ramify a great number of arterial vessels, *v*, or capillaries, *d*; these vessels are all extremely sinuous in the papillæ and at their bases. Magnified 60 diameters.

tumours. The modifications of these villi will be studied when analysing the lesions of chronic arthritis, the most frequent cause of these changes. In the *cerebral ventricles* we have seen cases of papillary neoplasms; these take their point of departure from the walls of the ventricles, and are formed of enormous composite papillæ completely covered with stratified and dentate pavement cells. Many of the papillæ show calcareous globes and fatty infiltration. The pavement cells covering the buds, partly disintegrated by cadaveric softening, form a whitish juice, so that a tumour of this kind might be mistaken for encephaloid carcinoma. The type of this singular pathological product may be found physiologically in the choroid plexus, composed of blood-vessels and vascular buds infiltrated with calcareous salts; the buds in the choroid plexus are also covered with pavement epithelium.

The diagnosis of papilloma is easily made in the majority of cases; but at times it is very difficult and can only be established after minute examination. To be certain that the tumour is a papilloma, neither the alveoli of carcinoma, nor glandular tracts, nor islets of epithelium should be found at the base of the papillæ. Now, a section, cut perpendicularly to the surface of a hardened papilloma, shows spaces between the papillæ at very different levels, the epithelial cells of which must not be mistaken for lobules of epithelioma; it is easy to make the distinction; for the latter penetrate far into the corium or submucous tissue, while the deepest of the interpapillary spaces of papilloma are almost on the same level as normal papillæ. On the other hand, if a transverse section of papilloma be cut rather obliquely, the interpapillary spaces, divided obliquely at their bases, resemble and may be mistaken for lobules of epithelioma. To be warned of the possibility of such an error is to avoid it, by making good preparations. The diagnosis is only possible under this condition.

The prognosis of papilloma is generally not serious, but by their seat they impede the performance of important functions—papillomata at the neck of the bladder for instance. In some cases, happily very rare, they become the point of departure of epithelioma.

III. Adenoma.

Adenomata correspond exactly to the glandular hypertrophies described by Lebert; they have been confounded with a great many other tumours under the name of *adenoid tumours*, *polyadenomata*, *heteradenomata*, &c. We consider adenomata to be tumours having the same structure as glands. Glands are divided into—1, racemose glands; 2, tubular glands, which latter may be again divided into those lined with a pavement and those with a cylindrical epithelium. In the same way adenomata may be divided into—1. **Acinous adenoma**; 2. **Tubular adenoma** containing cylindrical epithelium. Many French authors have also described an adenoma composed of glands containing pavement epithelium. But the existence of this species does not seem to us sufficiently established to be admitted in a definite manner without new facts being adduced to establish it beyond doubt.

1. **Acinous adenoma.**—Cruveilhier remarked that all tumours of the breast were not scirrhous, encephaloid, or colloid cancers, and he recognised a group of tumours which were hard or soft, yielding no juice and often encysted. These he called *fibroid bodies of the mamma.* Velpeau supposing that these tumours were caused by blows on the breast, a customary etiology to which all patients refer tumours, thought that they were caused by extravasations of blood which underwent ulterior modifications, and he gave them the name of *fibrinous tumours.* It was only later, when Lebert had discovered the glandular acini of these tumours, that Velpeau called them *adenoid tumours*, a name which does not distinctly signify that these tumours are formed of glands, but simply of a tissue having a glandular appearance. Lebert described them in his great work under the name of *hypertrophies of the mamma.* According to Broca (Art. 'Adenoma' in the *Dict. Encyclo.*) all that Cruveilhier called fibroid bodies of the breast and Velpeau adenoid tumours, are adenomata. The truth is, however, not as simple. We have in fact often examined tumours which had been diagnosed as adenoid by Velpeau, and have found them to be sometimes massive or papillary fibroma of the breast (p. 166) or sarcoma (p. 140) or myxoma, and sometimes, but very rarely, true adenoma. In describing fibroma, myxoma and sarcoma of the breast, we drew attention to the peculiarities they present when located in the breast, the growths they cause in the galactophorous ducts and acini, and the round or lacunar cysts with which they are riddled.

Adenomata of the breast are small and generally blended with the glandular tissue, while well-defined tumours quite distinct from the gland are generally fibromata, myxomata or sarcomata. They vary in size from that of a hazel nut to a walnut and are rarely larger. They contain no lacunar cysts, so that if these are present, far from characterising adenoma they eliminate it altogether. They are composed of acini arranged side by side, and separated by a small quantity of fibrous tissue. These acini are bounded by a well-defined membrane, which is lined with a regular epithelium. The development of these tumours is very slow and they never cause secondary growths. It has been suggested that they may become converted into carcinomata. This hypothesis is not based on well-authenticated facts. Lesions analogous to those of the breast may occur in other acinous glands, such are certain tumours of the parotid gland, hypertrophy of the lacrymal gland of which Lebert reports a case. The velum palati and the pharynx may also be the seat of tumours caused by considerable hypertrophy of the acinous glands they contain. These tumours are sometimes solitary and prominent, at others diffused and cause a general uniform thickening of the mucous membrane.[1]

Diagnosis of acinous adenoma.—In making the diagnosis of acinous adenomata they must be distinguished from all new growths, which by developing in the neighbourhood of glands cause a proliferation of the epithelium of their acini. Thus in acute or chronic laryngitis, at the same time that proliferation of the connective tissue of the mucous membrane takes place there is an increase in the size of the glandular acini, so that many attain double or triple their normal volume. They are also filled with epithelial cells, some arranged regularly against the wall, others free in the lumen of the gland, and in a state of fatty or colloid degeneration. Similar changes are met with in other mucous membranes. The glands of Lieberkühn of the intestine are, for example, always much hypertrophied adjacent to the Peyer's patches which are not yet ulcerated in typhoid fever. It is evident then that these appearances are the consequences of inflammatory irritation of glands, and not of adenomata. In tumours hitherto described, we have seen that every neoplasm affecting the stroma of a gland is accompanied, at a certain moment, with proliferation of the epithelial cells of the acini and excretory ducts, followed by dilatation of these cavities, and by various ulterior modifications of their contents. For example, every chondroma of the parotid causes proliferation of the glandular epithelium, and yet no one dreams of including these tumours among adenomata or epitheliomata. In tumours when the glands hypertrophy at the commencement and in the adult condition of the neoplasm, they soon undergo various changes, such as fatty or colloid degeneration of their epithelial cells, changes which often end in the formation of cysts or in atrophy of the acini. But when a tumour containing many hypertrophied glandular acini, a sarcoma of the breast for example, recurs after removal, the new growth generally contains no glands; an evident proof that the tumour was not adenoma, and that the hypertrophy of the glands in the primary tumour was an accessory fact. If the primary tumour had been an adenoma, the new growth on relapse in situ would have had the structure of adenoma. Such cases are common. Another example may be found in tumours of the testicle, called cysto-sarcoma or cystic tumour. When these tumours become generalised, the secondary growths in the lymphatic glands, peritoneum, lungs, &c., are found to have simply the structure of sarcoma. It is only by exact knowledge, and by an attentive examination of each case, that true adenoma can be recognised. The diagnosis may be established by the complete resemblance in structure and arrangement of the culs-de-sac with those of the gland attacked, by the outline of the acini, and finally by the nature of the inter-acinous tissue. We may add moreover that no tumour is more rare than true acinous adenoma.

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[1] In a case of this kind examined by ourselves the velum palati measured no less than one centimetre in thickness, and the glands, perfectly distinct and alone the cause of the thickening, showed their acini normally opening by the aid of ducts on to the surface of the mucous membrane, as in the physiological state. In this case the epithelial cells of the saccules presented physiological characteristics.

II. **Tubular adenoma with cylindrical cells.**—These tumours are very common in mucous membranes containing tubular glands. They result from general hypertrophy and budding of these glands, which hypertrophy causes a thickening of the mucous membrane and often even polypoid projections. The tumour is soft, generally but slightly vascular, and rather translucid. Superficially it has the same colour as the mucous membrane. On section it yields no milky juice, but a mucous fluid in which, under the microscope, cylindrical cells are seen isolated or united into flakes, also round and chalice cells. After hardening the specimens in alcohol or chromic acid, the sections obtained have a very different appearance according as the tubes are divided longitudinally or transversely. The longitudinal sections show the tubes lengthwise, often presenting lateral buds or true bifurcations, and either opening on to the surface of the mucous membrane or terminating in culs de-sac situated at different levels

These tubes are generally situated so close together that there seems to be no fibrous stroma. In other cases the latter is rather thick. The tubes are very often dilated in places. The epithelium which lines them is distinctly cylindrical. Its component cells are two or three times longer than is normally the case in the same glands; they have generally the same characters as chalice cells, that is to say, they are filled with mucus. It is

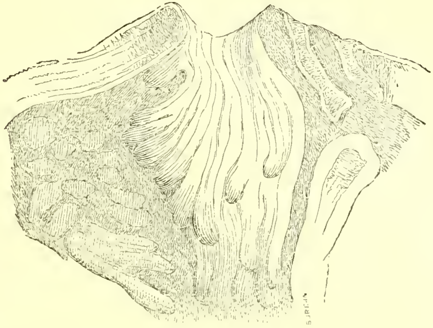

FIG. 166.—TRANSVERSE SECTION OF A SMALL POLYPOID ADENOMA OF THE SMALL INTESTINE.
Magnified 20 diameters.

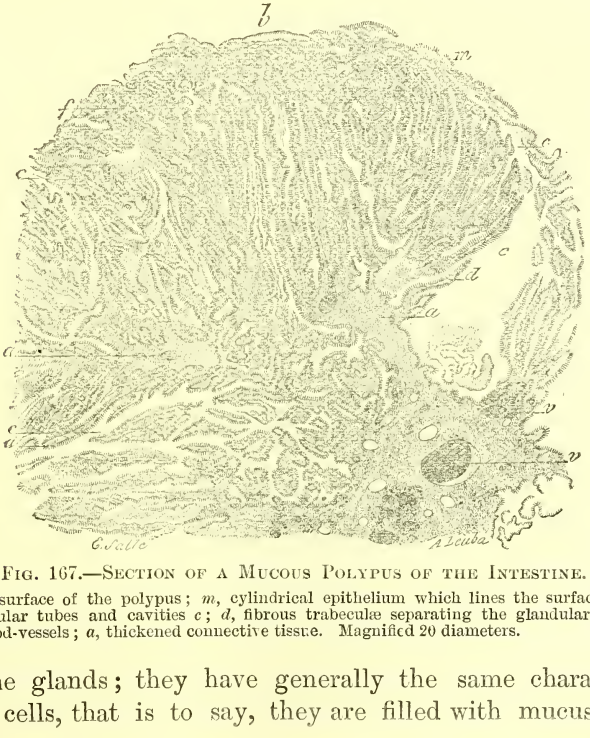

FIG. 167.—SECTION OF A MUCOUS POLYPUS OF THE INTESTINE.
O, free surface of the polypus; *m*, cylindrical epithelium which lines the surface of the glandular tubes and cavities *c*; *d*, fibrous trabeculæ separating the glandular tubes; *v*, blood-vessels; *a*, thickened connective tissue. Magnified 20 diameters.

particularly at the dilated points of the glands that chalice cells are observed. The tubes cut across transversely appear like circles with a regular border of chalice or cylindrical cells round a central lumen. The dilatation of the glandular tubes constitutes the first phase in the formation of cysts filled with colloid substance, and which are common in these tumours. The ovules of Naboth (fig. 168), which result from modifications of the tubular glands of the mucous membrane of the uterus, are almost the physiological type of these cysts.

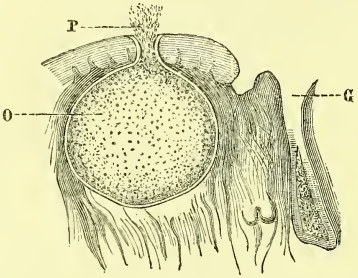

Fig. 168.—Ovula Nabothi from the Vaginal portion of the Cervix Uteri.

O, spherical dilatation of a gland the orifice of which opens at P; G, tubular gland. Magnified 20 diameters.

Seat of cylindrical-celled adenoma.—Hypertrophied glands of the *gastro-intestinal mucous membrane* are found rather frequently; in the stomach, the hypertrophied glands may be changed, by the plugging of their orifice with mucus and the retention of their secretion, into small cysts resembling the ovules of Naboth. Scattered through the mucous membrane irregularly, or in well-defined spots, various sized vesicles, which have taken the place of tubular glands or parts of them, may be met with (fig. 169). These hypertrophied glands and cystic vessels may form small tumours which often become pedunculated and form polypi. In the *uterus*, these mucous polypi may project into the vagina as far as the vulva, and as in the stomach (*vide* mucous polypi of these organs) hypertrophied glands may often combine with papillary neoplasms (*vide* fig. 170) to form composite tumours, villous on their surface, cystic and glandular throughout the rest of their mass.

Similar tumours are developed in the *rectum* and *small intestine.* In these the glandular buds springing from the terminal extremities of simple glands may be seen to give origin to new acini, so that glands originally tubular are changed into composite glands. It is seen, however, that these glands do not deviate from their primitive function, and that they continue to open on

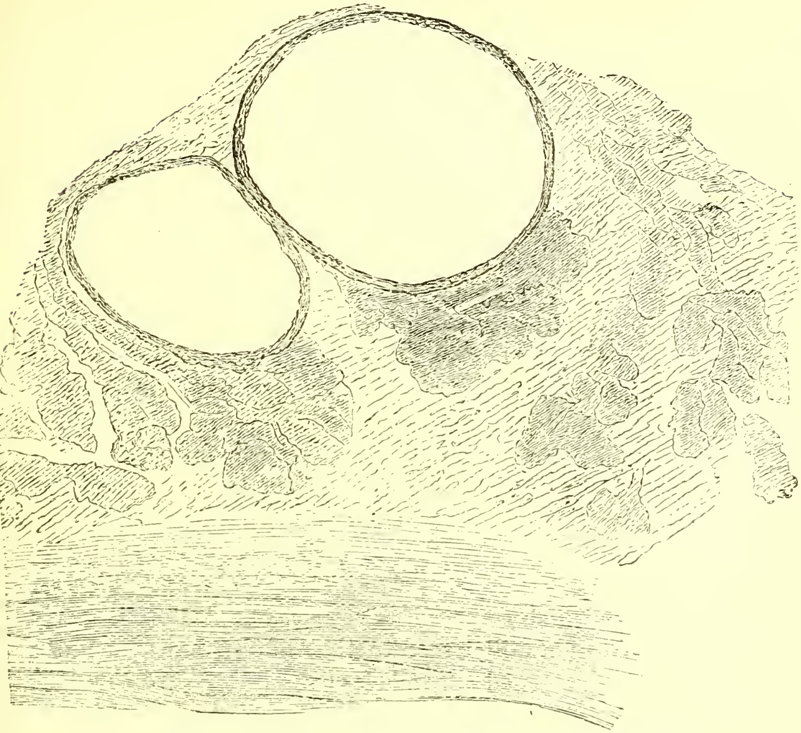

FIG. 169.—CYLINDRICAL-CELLED ADENOMA OF THE STOMACH.
Figure borrowed from Virchow.

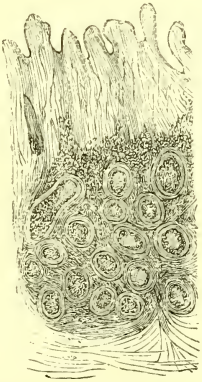

FIG. 170.—CYLINDRICAL-CELLED ADENOMATA OF THE STOMACH with A VILLOUS CONDITION OF THE SURFACE OF THE TUMOUR.
Magnified 20 diameters.

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to the surface of the mucous membrane and pour out the products of secretion. They may nevertheless, as in the preceding cases, give origin to small cysts. The stroma of the tumour is fibrous in the parts completely developed, and embryonic in the parts where the gland is budding. If the tumour developed in the rectum projects after pediculisation at the anus, the investing layers of epithelium change their character, the cylindrical cells being changed into pavement cells, which may even on the surface undergo horny degeneration. In the projecting parts in contact with the air, the glandular depressions are filled with stratified pavement cells, and the inter-glandular projections present thenceforth the appearance of papillæ, so that a layer of tubular glands may be seen to be transformed into a layer of papillæ covered with squamous epithelium. In the *uterus*, besides the vesicular changes of the glands we have indicated, glandular growths are seen characterised principally by hypertrophy of the glands of the cervix. These tumours are small, enclosed in the cavity of the cervix, or they may project through the os uteri into the vagina. Described by Huguier under the name of *mucoid cr utero-vesicular polypi*, they appear as red, soft masses, over which transparent vesicles are scattered, varying in size from that of a millet seed to that of a grape stone, or as fleshy, sometimes flattened appendages; the latter have superficial projections and depressions like the arbor vitæ. In structure, they greatly resemble the mucous membrane of the cervix, only that the parts are considerably hypertrophied. The folds lined with cylindrical epithelium are deeper and more numerous, the cylindrical cells are longer, and the glands dilated and branching. Sometimes the glands are not distended into cysts, in which case the name of utero-vesicular polypus is not applicable. Most frequently, however, the glands have numerous cystic dilatations throughout the thickness of the morbid mass. The stroma of these tumours is habitually formed of succulent fibrous tissue, permeated by numerous and dilated blood-vessels. Sometimes smooth muscle cells are also met with. These uterine polypi are covered with cylindrical epithelium in the cervix, with pavement cells in the vagina, and when projecting externally, which is very rare, with horny epithelium. But these changes of form of the superficial epithelium do not extend to cells lining ducts of the tubular glands, nor even to the depressions similar to the folds of the arbor vitæ which these polypi sometimes show. Polypi of the *nasal fossæ* are also met with, formed of arborescent papillæ, covered and surrounded with pavement epithelium.

Diagnosis of cylindrical-celled adenoma.—Among nasal polypi there are some so similar to cystic adenomata of the uterus that it is impossible to distinguish between them, even after microscopic examination. We have seen cases of this kind, in which the glands lined with cylindrical epithelium, and the cystic dilatations perfectly resembled uterine tumours previously described. The most frequent form of nasal polypus is, as we have already pointed out (p. 157), formed of mucous tissue, and is a myxoma, even when it contains hypertrophied and cystic glands. The only tumour with which cylindrical-celled adenoma may be confounded is cylindrical-celled epithelioma. In the immense majority of cases the diagnosis is easy; the regularity of the glands, their opening on to the surface of a mucous membrane, the presence of small regular cysts, establish it with certainty. In cylindrical-celled epithelioma small regular cysts are never present, there are only aberrations of the forms of tubes and cells removing them from the normal type. Epithelioma moreover invades the deep tissues, whereas adenoma is always well defined and superficial, and has a tendency towards the polypoid form.

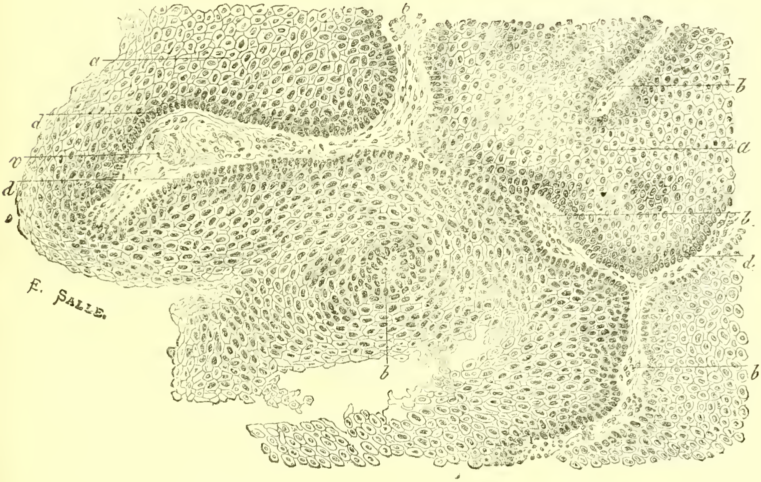

Fig. 171.—Papillary Polypus of the Nasal Fossæ.

a, pavement epithelial cells of which the most deeply placed, *d* are cylindrical and implanted on the papillæ, *b*. The latter have blood-vessels, *v*. Magnified 80 diameters.

While the **prognosis** of cylindrical-celled epithelioma is most serious, that of tubular adenoma is always benign. It never causes secondary growths, and does not recur if completely removed.

IV. Cysts.

We make use of the word *cyst*, sanctioned by usage, instead of *cystoma*, for the latter has no greater value and its radicle represents no tissue. We look upon cysts as glandular aberrations which, as regards structure, have, up to a certain point, their analogues in the composite glands of the closed vesicles, such as the thyroid body of the adult and the ovary. The vesicles of these glands are in fact formed of a wall of connective tissue, lined by epithelium, and containing in their interior fluid or colloid substance. Cysts are also formed of a membrane of connective tissue, with internal epithelium lining and fluid, mucous, colloid or sebaceous contents. They should be carefully distinguished from the mucoid degeneration accompanying the formation of cavities in the tissue of the various kinds of tumours previously described. In these tumours the cyst is never surrounded by a proper membrane, and has no internal epithelial lining. The analogy of cysts with glands is enforced by the fact that cysts are often nothing else than portions of excretory ducts or glandular saccules, the orifices of which have been plugged. But it must not be thought that retention, consequent on plugging of the glandular duct, is the sole cause of the accumulation of secretions in cysts. The phenomena are not so simple; for on tying the duct of a gland, far from cystic dilatation, atrophy is caused. The various cysts differ so greatly in their structure and mode of development that it is impossible to give a general description; hence, we will pass on at once to consider the nature and seat of the various kinds of cysts. The most natural division of cysts would be that based on their development, and they could then be divided into two groups, according as they originate from a natural cavity, or are formed *de novo* in the solid parts of a tissue or organ. But this division is impossible, for the mode of development of all cysts cannot be ascertained in an absolute manner. We therefore divide cysts according to the nature of their contents into two groups.

1. Sebaceous cysts.
2. Serous, mucous, and colloid cysts.

Group I.—Sebaceous Cysts.

Sebaceous cysts are divided into simple *sebaceous cysts* and *dermoid cysts.* The first consist in an accumulation of epidermic cells, or the product of secretion in a hair follicle or glandular duct.

A. Among sebaceous cysts may be distinguished :—

a. Those little whitish spots prominent on the skin of the face, particularly at the external border of the eyelids and on the cheeks, called **millet grains** or **milium palpebræ.** They are caused by an accumulation of epidermis in the hair follicles. The orifice of the hair follicle is obstructed, and it is only by incising the little granule that a ball of horny epidermic cells can be turned out. The cells at the centre are often dissociated, while superficially they are arranged in solid layers. These little tumours are really cysts of retention. They are extremely common.

b. **Comedones** are little elevations on the skin formed by the retention of sebaceous matter in the hair follicles. The orifice is patent, so that the contents can be squeezed out. In this sebaceous matter *demodex folliculorum* is sometimes found. The accumulation of sebum often causes inflammation of the follicle; pus cells are then mixed with the epithelial cells and fat droplets which constitute the sebum. It is thus that pustules of acne are formed.

Wens, frequent in the scalp, are caused by an accumulation of epidermic and sebaceous masses in the hair follicles. They may attain a considerable size, from that of a nut to a pigeon's egg; they are generally flat or lenticular. According as their contents are fluid or solid they are said to be *meliceric* or *steatomatous.* The contents, when meliceric, are fluid, resembling honey and composed of a quantity of free, fatty particles and dissociated epidermic cells. In steatomatous wens the contents are formed of the same elements, but there is less free fat and there are more epidermic cells. In wens, fat undergoes changes typical of malnutrition, and crystals are formed of stearic acid, margarin and cholesterin, always met with in more or less abundance. On the surface of the wen a black depressed spot is often seen, this is the orifice of the distended hair follicle; but it is often absent. The cyst is located in the subcutaneous tissue; the skin which covers its surface is thinned; the papillæ are flattened or have even disappeared so that the surface of the wen is consequently smooth. Neighbouring sebaceous glands are atrophied; finally the layer of subcutaneous adipose tissue beneath the cyst disappears. The wall of the wen is formed of connective tissue with flat cells (*a*, fig. 172), and parallel lamellæ of ground substance, a tissue comparable to the tunica interna of the arteries or to flat-celled fibroma (p. 163). This formation of the cyst wall (fig. 172) is caused by the pressure exercised on the wall, in consequence of the incessant accumulation of secretion in the cyst. In this membrane there are no elastic fibres, but they may be seen in the adjacent tissue. Fatty, calcareous, and atheromatous changes are very common in this layer of flat-celled connective tissue, which fact completes the analogy of this membrane with the tunica interna of the arteries and the fibromata previously indicated. On the internal surface of this membrane there is a lining of stratified pavement epithelium, which undergoes an evolution similar to that observed in the sebaceous glands. The cells in contact with the wall have large nuclei surrounded by a small quantity of protoplasm (*b*, fig. 172) (it is probably from these that the new cells are continuously developed); the cells then enlarge and become truly tesselated, soon their nuclei atrophy and disappear (*c*, fig. 172) and are replaced by droplets of fat (*d*, fig. 172). In some cases this fatty degeneration takes place slowly, and the layer of cells deprived of nuclei is thick; it may become detached from the wall of the cyst and form a shell composed of whitish tissue, slightly translucid and almost cartilaginiform. It is in the interior of this shell that the meliceric or steatomatous contents are found.

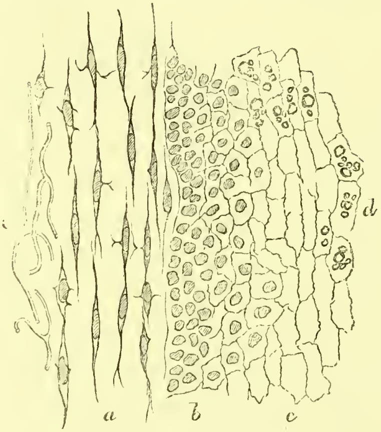

FIG. 172.

a, fibrous wall of the cyst formed of flat plasmatic cells; *e*, elastic fibres; *b*, epithelial cells; *c*, horny cells; *d*, sebaceous cells. Magnified 300 diameters.

B. **Dermoid cysts,** which contain like the preceding meliceric or steatomatous matter, are developed outside of glands and are characterised by a wall, the structure of which is analogous to that of the skin. Three varieties of these cysts may, according to Lebert, be recognised.

1. **The first variety of dermoid cysts** closely resembles wens; there is the same structure of the envelop, the same epithelial layer, and the same arrangement of the contents. The sole difference is in their seat; they develop in regions where there are no sebaceous glands, and they have no orifice.

2. In the **second variety,** the cystic membrane, which resembles the corium by its papillæ, has besides sebaceous glands and hair follicles. These follicles produce hairs and even locks of hair; and in the interior of these dermoid cysts, matted tufts of hair are generally found in the midst of sebaceous matter. The papillæ of the cystic wall may give origin to warts, chondromata (Bärensprung), and horny masses (Förster). The latter, developing at a point on the deep surface of the dermoid cyst, may extend and project externally, in which case they are surrounded at their bases by the cystic membrane, like a calyx.

3. **Lebert's third variety of dermoid cysts** is more complicated. Many different tissues, and even organs such as the teeth, may be found in the cyst wall, the contents of which are, as in the preceding varieties, composed of sebum. The teeth are found in a dental follicle in the midst of fibrous tissue, or they are implanted on bones of different forms. Their arrangement is very irregular, their development does not, according to Kohlrausch, differ from the normal type. These teeth have the characters of those of the first and second dentition, they are canines, molars, and incisors. There may be one or many teeth; in some cases their number is so great that Reil and Autenrieth have counted three hundred. This observation destroys the hypothesis put forth by some authors that these cysts are due to fœtal inclusion, for if it were a case of simple fœtal inclusion, it is not comprehensible how the teeth could be so numerous. Instead of an osseous plate for the insertion of the teeth an osseous ridge representing an alveolus is sometimes met with. Teeth and osseous tissue in the form of plates are what are most commonly found in the walls of these cysts, but long bones, irregularly arranged cartilaginous tissue, masses of striated muscular tissue, and even medullated nervous tissue may be seen. We have seen cysts of this nature in which nervous tissue, characterised by

delicate and medullated tubes and nerve cells, was contained in a fibrous pouch adjacent to osseous parts. Nothing is indeed more irregular than the arrangement and the relative quantity of these various tissues. In the cyst wall may be seen in places plates having the same structure as the skin, with papillæ, hair follicles, sebaceous and sudoriparous glands, and at other points the wall may be thin, smooth, fibrous, similar to that of cysts of the first variety. The size of these tumours varies between that of an egg and the head of an adult. Their mode of development is unknown. All that is known is that they are congenital, and date from intra-uterine life. Their most frequent seat is the ovary and the testicle; but they may be met with in other organs.

Group II.—Serous, Mucous, and Colloid Cysts.

The second group of cysts is characterised by their contents, which may be serous, mucous, or colloid. They may be developed (*a*) in the natural cavities belonging to the serous membranes, as for example in the subcutaneous, tendinous, or peri-articular bursæ, connected or not with the joint; (*b*) in glandular cavities; (*c*) or they may originate *de novo*. We will rapidly indicate the regions where they are found, and the varieties which may be distinguished, referring the reader to the organs where they are described with greater detail.

a. The serous cavities may be considered as hollowed in the midst of the connective tissue which surrounds the organs; they are lined with an endothelium which corresponds to the cells of the connective tissue, and which may be destroyed and renewed. Thus we should not be surprised to see regular or loculated accidental cavities, lined throughout with an endothelium, develop anywhere in loose connective tissue. In the physiological condition the membrane of these cavities secretes a serous fluid which is reabsorbed with the greatest facility by the blood-vessels. This facility of absorption is shown by the rapid disappearance of fluids injected into these cavities. But if the serous membrane is inflamed, the absorption of the injected fluid is impossible (Rindfleisch), and further the irritation of the serous membrane causes an abundant secretion. A slight irritation suffices then to transform a serous bursa into a cystic cavity. Such a subcutaneous serous bursa transformed into a cyst is called a **hygroma.** This lesion may be classified with tumours by reason of its tendency to persist indefinitely, though it is generally of inflammatory origin. Many other tumours have also an inflammatory origin, for example, exostoses and lamellar fibromata. The cystic membrane of hygroma is generally thick, formed of dense connective tissue of cartilaginous appearance. According to Virchow hygroma is always lined by pavement epithelium. The contained fluid is transparent or rendered slightly cloudy by the presence of free cells ; it sometimes contains concretions of very irregular form—riziform bodies—composed of concentric layers without histological structure. The origin of these bodies is variously interpreted ; Virchow considers that they are caused by budding of the cyst wall. In structure the sheaths of tendons strongly resemble subcutaneous serous bursæ, as they are formed of a layer of connective tissue, both the tendon and the opposing surface being lined with a layer of endothelium. They have also, according to Gosselin, little glove-like depressions which penetrate into the adjacent connective tissue. Obliteration of the neck of these prolongations causes the production of little cysts connected with the sheath of the tendon and called ganglions ; they are chiefly observed at the wrist and on the instep. In structure they resemble hygroma and often contain riziform bodies. Hydrocele of the tunica vaginalis and effusions into the synovial membranes may be classed with the preceding cysts, as they appear to have a similar origin. These cases are intermediate between chronic inflammation and tumours, and may be included under one or other head.

b. **Cysts developed from glands** are very numerous. The thyroid body in the normal condition contains cysts filled with colloid matter, which is produced by the evolution and colloid transformation of cells within these cavities. The Graafian follicles of the ovary, even in new-born infants and before menstruation, are often filled with and distended by a large quantity of fluid, constituting a dropsical condition of the follicles (see ovary), and it is probable that a certain number of ovarian cysts originate in this manner (Förster). The mucous glands of the lips may by retention of their secretion be transformed into small transparent cysts ; they are then, according to Virchow, comparable to the millet granules and comedones of the hair follicles. The buccal mucous membrane may be raised from the floor of the mouth by voluminous cysts, resulting from the distension of the ducts of Wharton and Rivinus ; these are called *ranulæ.* In the stomach, intestine, and trachea are found small isolated acuminated mucous cysts resulting from the distension of tubular and acinous glands. In the liver, cysts are sometimes found containing bile, bile pigments, or simply serum. These solid or fluid substances accumulate in the dilated bile ducts above an obstacle to the free flow of the bile. The kidney is frequently the seat of cysts the cause and origin of which are variable. Such are the congenital cysts, often very large, arising, according to Virchow, from atresia of the papillæ. He has found urates in the fluid of these cysts, and we have found urea in the same. In the adult,

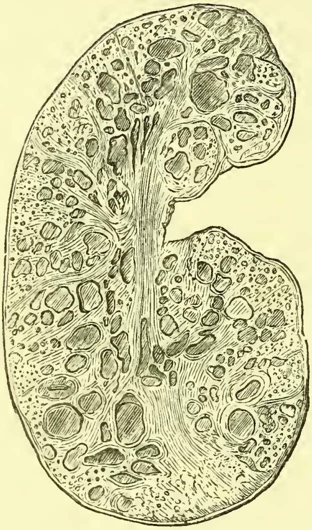

Fig. 173.—Congenital Cyst of the Kidney.
After Virchow.

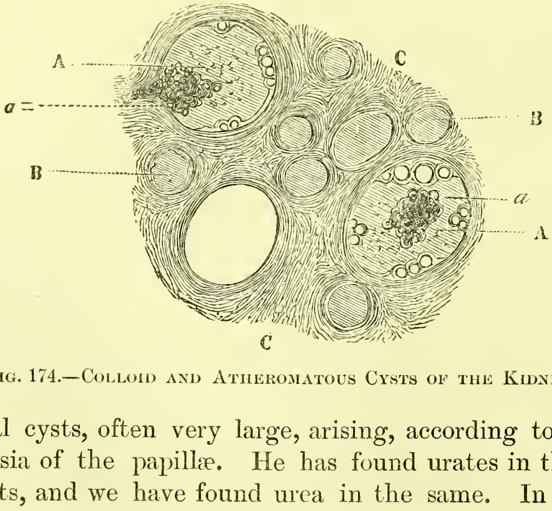

Fig. 174.—Colloid and Atheromatous Cysts of the Kidney.

serous or colloid cysts may also be found as the result of Bright's disease or interstitial nephritis, and which contain either serous or colloid matter ; they are produced by distension of the uriniferous tubuli, or of the capsules of the glomeruli (*vide* cysts of the kidney). In the testicle, there are often similar growths, either outside of the glandular elements, or springing from the hydatids of Morgagni, or from distended seminiferous tubes. They frequently contain spermatozoa (*vide* cysts of the testicle). The cystic growths of the uterus are almost normal in what are known as the *ovulæ Nabothi*. In the mamma, there are, according to Virchow, cysts which are developed from the galactophorous ducts ; they are sometimes filled with caseous detritus, and are often so distended that before opening them it might be thought that they were solid tumours. Similar productions are also found in various mammary tumours.

c. **Cysts formed de novo**, that is, not resulting, as the preceding, from distension of pre-existing cavities, have the following characteristics : 1. In the subcutaneous or deeply seated connective tissue they are sometimes formed of a delicate membrane containing serous fluid, sometimes of a thicker, irregular, and anfractuous wall lined with a cylindrical and ciliated epithelium. Förster has observed a lining of ciliated cells in certain cysts, and M. Dumoulin has described peri-laryngeal and peritracheal cysts with a similar investment ; we have also seen many cysts with ciliated epithelium, notably in a case of proliferous cyst of the peritoneum. 2. In the muscles, tendons, bones, brain, &c., these cysts are occasionally found, but are very rare. 3. In the ovaries, where they are very frequent, they form the variety called proliferous cysts. From the researches of Pflüger and Waldeyer, it has been ascertained that the ovules spring originally from the cells of the investing epithelium of the peritoneum covering the ovary. The epithelium on the surface of the ovary sends into the stroma of that organ solid, epithelial buds which proliferate there and become isolated, ultimately forming the Graafian follicles, which are simply therefore physiological cysts developed from the germinating epithelium covering the ovary.

Proliferous cysts appear also to originate from the epithelium covering the surface of the ovary. This opinion, first maintained by Waldeyer, has been lately strengthened by the researches of MM. Malassez and De Sinéty. According to these observers, epithelial buds, analogous to those which form the tubes of Pflüger in the embryo, are produced on the surface of the ovary and penetrate its stroma; they grow, ramify, become hollowed, and form culs-de-sac lined with epithelium. The epithelial cells lining the interior of the tubes are cylindrical, cubical, ciliated, or caliciform, &c. This variety of form in the cells distinguishes them from those lining the tubes of Pflüger and the Graafian follicles. The internal surface of these newly formed cavities, which are destined to become the starting-point of proliferous cysts, is villous, and from the investing epithelium are given off epithelial buds and growths, which penetrate the walls and tend to become the starting-points of new cysts. These proliferous cysts have characters which distinguish them from all preceding varieties; they are met with most frequently in the ovary, but occasionally also in the great omentum; they may attain an enormous size, being the largest cysts known in human pathology. They are all multi-locular, and have thick walls independent of one another or common to many cystic cavities. Their internal lining resembles mucous membrane, and has papillæ and villi arranged in more or less extensive islets; finally,

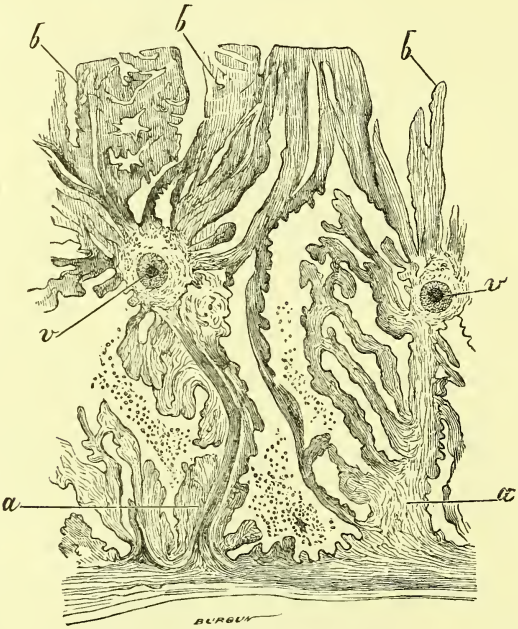

FIG. 175.—TRANSVERSE SECTION OF THE WALL OF A PROLIFEROUS CYST OF THE OVARY.

a, ramifying buds and papillæ limiting sinuous spaces; *b*, papillary surface; *v*, blood-vessels cut across. Magnified 20 diameters.

in their walls secondary cysts are formed. The tissue which separates and unites these different cysts is most frequently a young and very vascular connective tissue, in some places entirely embryonic. In a few cases we have found mucous tissue. The papillæ or villi springing from the internal surface of the cysts are simple or compound; their arrangement is often very complicated, as is shown in fig. 175; in the centre they are formed of embryonic connective tissue: their blood-vessels are numerous, and often dilated in an ampullar manner; sometimes they rupture and cause ecchymotic spots—the blood may even be effused into the cavity of the cyst, which fact explains how the fluid contained in ovarian cysts is often more or less blood-stained. The papillæ and the internal surface of the cysts are lined with epithelial cells, which are sometimes small and cubical, but more often by chalice cells, or by cylindrical cells, which may be ciliated or not. In the various layers of the walls of these cysts, particularly in the papillary layer, small cysts are observed varying in size from a pin's head to that of a nut, exactly similar to the parent cyst. Ovarian cysts contain a serous or colloid fluid, sometimes colourless, but often stained red or a more or less dark brown. In it are found regular or deformed epithelial cells, in a state of colloid or granular fatty degeneration and undergoing destruction, free fat granules, and often cholesterin crystals, which may be present in such numbers that they may be seen to glitter in the fluid. When the fluid is coloured, red blood-corpuscles variously altered, granules, and crystals of hematoidin are found.

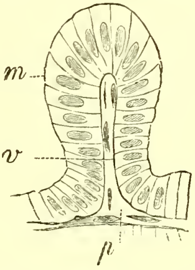

FIG. 176.—BUD FROM THE PRECEDING PREPARATION MAGNIFIED 300 DIAMETERS.

v, blood-vessel; *m*, cylindrical epithelium.

The development of the secondary cysts has been studied by Förster and Wilson Fox with very different results. Förster found in the thickness of the wall of the primary cysts, islets of indifferent cells the most internal of which undergo colloid degeneration and are destroyed, while those at the periphery persist and constitute the epithelial lining of the cystic cavity. According to Wilson Fox, secondary cysts are formed by the free ends of the papillæ and villi becoming welded together, leaving at their bases cystic cavities lined by a continuation of the same epithelium. Such is the mode of development represented at fig. 175. We do not deny the possibility of the mode of production indicated by Förster, but we are bound to say that we have been unable to follow it in a satisfactory manner. Thus, we have observed round islets of embryonic tissue in the walls of cysts, but we have been unable to trace the transformation of these into true cysts. We are aware that MM. Malassez and de Sinéty think that secondary cysts are developed by epithelial buds and glove-like depressions, passing from the internal surface into the connective tissue of the wall, and it is reasonable to think that secondary cysts spring from the surface of a cyst already formed in the same manner as primary cysts are developed from the epithelium which covers the ovary.

These tumours greatly resemble adenoma and papilloma, both as regards structure and character. In fact if a good preparation from the wall of an ovarian cyst be submitted for examination, without the observer being previously informed whence it was taken, hesitation would be felt in deciding if it were a proliferous cyst, an adenoma of the cervix uteri or of the nasal fossæ, a papilloma, or even a cylindrical-celled epithelioma. These tumours are also very similar to sarcoma developed in a gland, the mamma or testicle for example. But on examining the whole morbid mass doubt is no longer possible. Proliferous cysts may attain an enormous size and cause death, but they do not generally produce secondary growths like sarcoma or carcinoma. True cysts are included among mixed tumours.

XI. MIXED TUMOURS.

In the fœtus or new-born infant, large tumours are sometimes found formed of an embryonic tissue, which has undergone such an evolution that most of the tissues are represented.[1] These tumours in form, colour, and consistency resemble encephaloid carcinomata. In the midst of the embryonic tissue, which is permeated by blood-vessels with embryonic walls, are found, firstly, striated muscular fibres in the process of development; secondly, embryonic cartilage; thirdly, bone in the act of developing from cartilage: the cartilaginous and osseous masses are covered respectively with perichondrium and periosteum; fourthly, cysts with a well-defined membrane and internal epithelial lining formed of tesselated or cylindrical ciliated cells; fifthly, long tracts or tubes of cylindrical epithelium, or lobules of pavement epithelium. These tumours cannot be looked upon as fœtal inclusions, for there is nothing in them resembling the form of a fœtus. The name of *teratoma* which Virchow proposes to give them does not seem to us to be suitable, for though they are formed of various tissues in process of development as in the embryo, they have as a whole no fixed form recalling that of an added being. They have, on the contrary, the form of an enormous embryonic bud springing from the surface of a being undergoing development, and participating in the property, which at this age all embryonic tissue possesses, of forming every kind of organic tissue. These various tissues, muscular, osseous, &c., have a much less advanced degree of development than those in the subject bearing the tumour; so that supposing that the elements develop regularly, the date of their origin can be calculated. As new-born infants affected with these tumours soon die, it is not known what they might become later. These complex embryonic tumours may be strictly regarded as sarcomata developed in embryo; but owing to the multiplicity of the normal tissues met with in them, particularly by the presence of epithelial, cartilaginous, and muscular masses, they are distinguished from all sarcomata hitherto described.

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[1] We have had occasion to examine two voluminous tumours of this kind; one was presented to the *Soc. de Chir.*, with a histological note by Charles Robin, who considered it to be a heterotopia of the ovary. (*Soc. de Chir.* 1867.)

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ANATOMICAL DIAGNOSIS OF TUMOURS.

ANALYTICAL TABLE.

To determine the histological composition of a certain given tumour a hypothetical diagnosis is first made from naked-eye appearances. When made by an expert, this diagnosis is often verified by microscopical examination, or it is abandoned or modified according to the results of this examination.

In the following table the two kinds of appearances are set out, those seen with and those without the aid of the microscope.

CHARACTERS DISTINGUISHED BY NAKED-EYE EXAMINATION.

The tumour may be:—

A. Ossiform.
B. Cartilaginiform.
C. Soft, with a milky juice.
D. Soft, with a grumous juice.
E. Fleshy.
F. Adipose.
G. Gelatiniform.
H. Fibrous.
I. Black or melanotic.
J. Formed of granulations.
K. Caseous.
L. Papillary.
M. Cystic.
N. Erectile.
O. Complex; presenting at different points many of the preceding characters.

CHARACTERS DRAWN FROM MICROSCOPICAL EXAMINATION.

A. OSSIFORM TUMOURS.

Method of Examination.—On scraping an ossiform tumour it generally yields only a few angular fragments, which give on testing the reaction of carbonate of lime, but offer no precise histological characters. To ascertain the constitution of ossiform tissue sections should be cut by means of a saw, and ground down between two pieces of fine pumice-stone cut in the direction of their fibres and saturated with water. To demonstrate the vascular canals, which is useful in a great number of cases, the preparation must, after having been ground, be placed in an ammoniacal solution of carmine, allowed to dry, and then ground afresh, the pumice-stone being wetted with alcohol. In this way the walls of the Haversian canals alone remain coloured. Sections thus obtained should be examined in Canada balsam. To see the cells and nuclei contained in the acunæ the bone should be decalcified in chromic or picric acid, and sections cut and afterwards stained with picro-carminate or purpurin. When the tumour has ossiform trabeculæ or delicate needles they can be separated, withdrawn, and submitted at once to examination.

Microscopical examination enables us to ascertain the following peculiarities :—

a. Bone corpuscles situated in a laminated ground substance.	**Osteoma** (p. 225). **Ossifying sarcoma** (p. 141). **Ossifying chondroma** (pp. 217 and 222).
b. Granular, or very transparent, and non-laminated ground substance, in the midst of which are seen striæ or irregular lacunæ of unequal size, but which have a coarse resemblance to bone corpuscles.	**Calcified fibroma** (p. 165). **Calcified sarcoma** (p. 134). **Calcified myoma** (p. 234).
c. The same ground substance limiting small cavities which lodge globular elements, *i.e.* the cells of sarcoma or chondroma.	**Calcified sarcoma** (p. 134). **Calcified chondroma** (p. 221).

In sarcoma, fibroma, myoma, and chondroma it is rare for calcareous infiltration to be present throughout the entire mass of the tumour so as not to find parts in which the constituent tissue can be studied. Maceration of small fragments of these tumours in chromic or picric acid removes the calcareous salts, and allows of sections being cut in which the true histological structure can be studied.

B. Cartilaginiform Tumours.

Method of Examination.—These tumours may be studied by means of sections made in the fresh state; alcohol, chromic and picric acid are only employed as preserving or fixing agents. Solutions of iodine and picric acid are useful.

a. Cartilage cells and capsules; the different varieties of cartilaginous tissue (see p. 17)	**Chondroma** (p. 214).
b. Trabeculæ formed of a ground substance, which may be homogeneous or infiltrated with calcareous salts, containing angular corpuscles. These trabeculæ limit spaces filled with vascular connective tissue; they sometimes contain islets of hyalin or calcified cartilage	**Osteoid tumours** (p. 222).
c. Homogeneous ground substance arranged in lamellæ, between which are found elongated, flat, or fusiform cells, the flat and ovoid nuclei of which take the stain of carmine and become clearly apparent after being acted upon by acetic acid . . .	**Lamellar fibroma** (p. 163).

C. Soft Tumours yielding a Milky Juice.

Method of Examination.—To ascertain the presence of juice the tumour is divided, and the divided surface scraped, or else the juice is squeezed out by lateral pressure. This juice always contains cells and nuclei, which are, however, never sufficiently characteristic to define the species of tumour under examination. Every tumour containing juice should be hardened in alcohol, picric, or chromic acid, or in Müller's fluid, and afterwards by the successive action of gum and alcohol. Sections can then be cut, from which, if it is wished to make a careful examination of the stroma, the cells can be brushed away with a camel's-hair brush. Carmine, purpurin, and hæmatoxylin are used for staining.

a. Small round cells and reticulated stroma (p. 15)	**Lymphadenoma** (p. 247).
b. Cells round or irregular, small or large; stroma alveolar and fibrous	**Carcinoma** (p. 172).

While these two classes of tumours are found to contain juice immediately after removal, the following do not yield juice immediately after removal from the living subject, but it is present twenty-four hours afterwards, or when the tumour is removed from a cadaver.

c. Round or fusiform cells which are in contact, or separated by a slight quantity of a soft substance; the blood-vessels, the walls of which are embryonic, permeate the tissue in every direction	**Sarcoma** (v. E, *a*[1]).
d. Stroma limiting alveoli lined with cylindrical epithelium	**Cylindrical-celled epithelioma** (p. 273).
e. Stroma limiting ramifying tubes filled with pavement epithelium showing no epidermic evolution	**Tubular epithelium** (see D, *a*).
f. Stroma limiting lobules of various forms, composed of pavement epithelium, showing epidermic evolution	**Lobulated epithelioma** (see D, *b*).
g. Tumours of the mamma, testicle, and cervix uteri, which determine budding growths into the ducts. These growths and the tissue of the tumour itself are formed of	
fibrous tissue	**Fibroma** (p. 161).
mucous tissue	**Myxoma** (p. 154).
embryonic tissue	**Sarcoma** (p. 139).

D. Soft Tumours with Grumous Contents.

Method of Examination.—These tumours yield a grumous substance on scraping the divided surface. On this surface whitish spots or tracts are seen. The grumous substance is found under the microscope to be composed of epithelial cells joined together. To study these elements in an isolated state the tumour should be examined in the fresh state, or in sections cut after hardening, as described at C.

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[1] In this table we make use of two kinds of references, some to pages in the text and others to other parts of the table. For the latter we use two letters: a capital letter when referring to naked-eye appearances, and small letters to microscopic characters.

a. Stroma limiting ramifying tubes filled with pavement epithelium showing no signs of epidermic evolution	**Tubular pavement epithelioma** (p. 268).
b. Stroma limiting lobules of various forms, and which are composed of pavement epithelium showing epidermic evolution	**Lobulated pavement epithelioma** (p. 258).
c. Combination of the two preceding forms.	
d. Fibrous stroma usually containing no blood-vessels, closely surrounding lobules which show no epidermic evolution, but in the centre of which are epidermic pearls	**Pearly epithelioma** (p. 267).
e. Tumours of the breast, containing whitish tracts radiating from the nipple; these tracts, formed of epithelial cylinders, are located in the galactophorous ducts, and may be obtained by scraping. The rest of the tumour shows the characters of carcinoma	**Carcinoma** (p. 177).

E. FLESHY OR SARCOMATOUS TUMOURS.

Method of Examination.—These tumours, of the consistence of flesh, are grey or rose-coloured, homogeneous or fibrillar, semi-transparent and soft. They are examined in the same way as the preceding.

a. Cells round, irregular, or fusiform, small or large, containing one, many, or a great number of nuclei. Cells are arranged without order or are gathered into bundles; the capillaries are irregular, often without proper walls, and sometimes form a true lacunar system	**Sarcoma** (p. 126).
b. Smooth muscle-cells arranged in bundles, and separated by vascular loose connective tissue. It is difficult to separate the cells by scraping or by dissociation with needles; to effect this, maceration in nitric acid must be resorted to (vide MUSCULAR TISSUE, p. 26)	**Myoma** (p. 232).
c. Tumour composed of acini and glandular tubes, exactly like those of normal tissues	**Adenoma** (p. 283).

F. ADIPOSE TUMOURS.

Method of Examination.—The tumours, in appearance like adipose tissue, are semi-transparent, yellowish in colour, and contain brilliant oil globules.

The microscopical examination is made by means of sections cut from fresh or hardened specimens.

a. Typical adipose tissue; lobular arrangement; tracts of connective tissue and capillaries round adipose cells	**Lipoma** (p. 168).
b. In the midst of the adipose tissue are found more or less extensive islets of a gelatinous tissue, showing, under the microscope, all the characters of mucous tissue	**Lipomatous myxoma** (p. 155).
c. Tumours without stroma; generally very large. All the cells are in contact, and contain distinct fat droplets without there being any tendency to cellular destruction	**Lipomatous sarcoma** (p. 148).
d. Stroma alveolar; cells free in the alveoli, and contain fat droplets without there being any tendency to cellular destruction	**Lipomatous carcinoma** (p. 182).

G. GELATINIFORM TUMOURS.

Method of Examination.—These tumours, transparent in appearance, and of a remulous consistence like gelatine, yield on scraping a gummy juice, in which, on microscopical examination, are seen cells of various forms, debris of elements, a few granules, and fat drops. Their structure may be studied in sections cut from fresh or hardened specimens; as they are not hardened by chromic acid, recourse may be had to simple dessication. To make the isolated elements apparent it is well to stain them with a weak solution of iodine, or with carmine.

a. Tissue regularly formed of fusiform or stellate cells, anastomosing together and separated by an amorphous ground substance, permeated with blood-vessels. In some tumours there are in addition elastic fibres and fat vesicles	**Myxoma** (p. 154).
b. Tumours corresponding to the description of sarcoma (vide E, *a*). In some spots, where the morbid mass is destroyed it is replaced by a mucous, structureless substance, more or less fluid, and often containing the debris of cells, fat, and pigment granules	**Myxo-sarcoma** (p. 147).
c. Tissue fibrous, with mucous cavities and masses similar to the preceding	**Mucoid fibroma** (p. 164).
d. Stroma distinctly alveolar; the alveoli filled with a mucous mass generally containing cells in a state of colloid degeneration	**Mucoid carcinoma** (p. 182).

e. Cartilaginous tissue with generally anfractuous cavities filled with a mucoid substance; or else formed of a mucoid ground substance in which ramifying cartilage cells are found, or well-preserved capsules, as in the intervertebral discs	**Mucoid chondroma** (p. 217).
f. Alveoli irregular, often elongated, some filled with a mucoid substance in which round cells in a state of mucoid degeneration are suspended, as well as cellular debris and fat granules; others lined with cylindrical-celled epithelium and contain mucus. Alveoli are also found simply lined with cylindrical-celled epithelium	**Cylindrical-celled epithelioma in a state of mucoid degeneration** (p. 276).
g. Tubular epithelioma (vide D, *a*) with a mucous stroma	**Mucoid tubular epithelioma** (p. 270).
h. Lobulated epithelioma (vide D, *b*), in which the cells undergoing epidermic evolution are in a state of colloid degeneration	**Colloid lobulated epithelioma** (p. 261).
i. In the supra-renal capsules and lymphatic glands lacunar spaces are found filled with colloid masses having festooned borders. This arrangement, normal in the thyroid body of the adult, may be exaggerated so as to constitute a tumour	**Colloid cysts** (p. 296).

II. FIBROID TUMOURS.

A certain quantity of connective tissue enters into the composition of almost every tumour. If this tissue becomes very abundant, and the specific tissue of the tumour ceases to produce disseminated islets, the total mass takes a fibroid appearance, without it for all that being a fibroma. Thus every fibroid tumour requires a most attentive examination.

Method of Examination.—Sections cut from a fresh or a dried specimen, or one hardened by the reagents already mentioned. Staining with carmine, alone or after the action of acetic acid, is very useful in order to demonstrate the existence of connective-tissue cells.

a. Connective-tissue bundles intersecting in various directions, with or without blood-vessels. Lobulated arrangement	**Fibroma** (p. 161).
b. Tissue carcinomatous and alveolar; the cells contained in the alveoli are undergoing destruction, and may be even entirely absorbed	**Atrophic carcinoma** (p. 180).

c. Stroma fibrous and very abundant; in it are found epithelial tracts arranged as in lobulated, tubular, or cylindrical-celled epithelioma (vide D, *a*, *b*; C, *b*)	**Epithelioma** (p. 257).
d. Intersecting bundles of smooth muscle-cells, separated by fibrous tissue, and united in the form of lobules; always located in non-striated muscular tissue	**Lobulated myoma of smooth fibres** (p. 233).
e. Tissue which on dissection is found to consist of medullated nerve-tubes and drops of myelin. The tumour is always developed on the course of a nerve	**Myelinic neuroma** (p. 237).
f. Tumours composed of non-medullated fibres	**Amyelinic neuroma** (p. 237).
g. Whitish, caseous, and lardaceous masses, formed of elements undergoing atrophy and retrograde changes, surrounded by a thick fibrous zone, in which are irregular lacunæ filled with fat granules	**Syphilitic retrogressive gummata** (p. 187).

I. Black or Melanotic Tumours.

Method of Examination.—In appearance the tumour is either completely black, or slate-coloured, or a mixture of grey and black. It always yields a blackish or sepia-coloured fluid. On scraping only black granules are often obtained. The black spots of the tumour should be particularly examined. Delicate sections cut from fresh or hardened specimens are indispensable in order to make the diagnosis.

a. Pigmentary infiltration into the elements of the various physiological tissues (very rare in man)	**Simple melanosis** (see appendix to tumours).
b. Sarcomatous tissue (vide C, *c*)	**Melanotic sarcoma** (p. 148).
c. Carcinomatous tissue (vide C, *c*)	**Melanotic carcinoma** (p. 183).

Care must be taken not to confound melanotic granules, which are black from the beginning, with blood pigment, which takes different tints before turning black, or with fragments of carbon, which are angular, while melanotic granules are spherical.

J. Tumours formed of Granulations.

Methods of Examination.—Small spherical masses the size of a millet seed, isolated only by dissection or by dilaceration. Their structure is studied in sections made after hardening, as previously described.

a. Tissue composed of small cells, immersed in a fibrillar and resisting substance. The centre of the granulation is atrophied, and has generally broken down into a caseous detritus. The periphery of the granulation is formed of embryonic tissue	**Tubercular granulations (p. 202).**
b. All tumours which are capable of generalisation may determine the growth of small spherical masses, which are composed of tissue identical to that of the parent tumour. The diagnosis of the primary tumour will aid in making that of these growths	**Carcinoma, epithelioma, sarcoma, lymphadenoma, &c.**

K. Caseous Tumours.

Under this denomination are included all tumours in which the entire mass, or a part only, is composed of an opaque, whitish, or yellowish substance which recalls by its appearance and its consistence that of rotten cheese. They are either friable or have a firm, lardaceous feel. The nature of the degenerated tissue cannot be deduced from the microscopical examination of the altered parts.

a. Isolated granulations in a state of caseous degeneration	**Tubercular granulations (vide J, *a*).**
b. More voluminous masses, on the borders of which, and sometimes throughout their entire extent, tubercular granulations are found	**Confluent tubercular granulations (p. 208).**
c. Sarcomatous tissue (vide E, *a*), or carcinomatous (vide C, *b*, &c.), round the caseous mass	**Sarcoma, carcinoma, &c., in a state of caseous degeneration.**
d. Dense caseous masses surrounded by a fibrous zone (vide H, *g*)	**Syphilitic gummata.**

L. Papillary Tumours.

Methods of Examination.—Sections made for the study of papillary tumours must be cut quite parallel to the direction of the papillæ, else the inter-papillary spaces, filled with epithelium, appear like islets of epithelioma.

a. Fibrous tissue provided with blood-vessels constituting the body of the papilla, the base of which is formed of the normal tissue of the region	**Papilloma (p. 277).**
b. The body of the papilla, or the tissue which forms its base, is composed of sarcomatous tissue	**Papillary sarcoma (p. 150).**

c. Or of carcinomatous tissue	**Villous carcinoma** (p. 185).
d. Or of mucous tissue	**Papillary myxoma** (p. 156).
e. Or of lobules of epithelioma	**Papillary epithelioma** (p. 261).

M. Cystic Tumours.

True cysts, lined with an epithelium and possessing a proper membrane, must be distinguished from lacunæ filled with serous, mucous, or colloid matter, hollowed simply in the tissue of sarcomata, carcinomata, fibromata, chondromata, etc. The lacunæ lined with epithelium developed in tumours of the mamma, testicle, and many other glands we regard only as simple complications, and not as cysts. To make the diagnosis certain, the tissue surrounding the cystic cavity should be carefully examined.

a. Containing serous fluid	**Serous cysts** (p. 296).
b. Containing colloid substance	**Colloid cysts** (p. 297).
c. Containing epidermic cells and fat	**Sebaceous cysts** (p. 293).
d. Cysts the membrane of which is similar to the skin, and may even contain bones, teeth, muscular and nervous tissue	**Dermoid cysts** (p. 295).

N. Erectile Tumours.

All erectile tumours are not angiomata, this term only applying to tumours formed entirely of blood-vessels and of a stroma of connective tissue.

Method of Examination.—When these tumours are gorged with blood they should be hardened in absolute alcohol, concentrated solution of picric acid, Müller's fluid, or in gum and alcohol; sections are then cut, stained with carmine, and examined in glycerine rendered slightly acid with formic acid. The red blood corpuscles which fill the vascular spaces are not stained with the carmine, while the other cellular elements are rendered distinct by the colour.

a. Irregular lacunæ without proper walls and filled with blood, hollowed in sarcomatous tissue	**Erectile sarcoma** (p. 145).
b. Dilated capillaries in a tissue showing the structure of carcinoma	**Erectile carcinoma** (p. 181).
c. Dilated capillaries in a tissue showing the structure of smooth-celled myoma	**Erectile myoma** (p. 234).
d. Numerous and dilated vessels, separated by connective tissue, or by the tissue of the part in which the tumour is developed	**Simple angioma** (p. 239).
e. Cavernous spaces filled with blood, and separated by incomplete septa of fibrous tissue. If the blood has escaped the tumour has a spongy appearance	**Cavernous angioma** (p. 240).

O. Complex Tumours.

In various parts of its mass the tumour has different naked-eye appearances. Each of these parts has characters corresponding to one of the preceding divisions, and may be studied separately by proper methods. The examination of the tumour requires the greatest attention.

APPENDIX TO TUMOURS.

By a strict adherence to our definition of tumours we have been unable to include any description of circumscribed collections of pigment, nor of hydatid cysts. We have therefore added an appendix in which these may be briefly described.

Simple circumscribed melanotic masses in the form of tumours.

Synonyms.—These simple melanotic masses have often been confounded with melanotic carcinomata or sarcomata, under the name of *melanosis* or *melanomata.* Anxious to avoid a similar confusion we do not, to designate these masses, make use of the name *simple melanoma*, for the radicle is not representative of a tissue.

Definition.—The melanotic masses now under consideration are distinct from melanotic sarcoma or carcinoma, inasmuch as the melanotic granules do not accumulate, as in those tumours, in cells of new formation, but in the normal pre-existing elements. When melanotic pigment granules accumulate in the cells of a normal tissue (p. 75) the cells are destroyed, and, on the process of infiltration continuing, the tissue itself is destroyed, and replaced by a nodule or tumour softened at the centre. We give the name of **melanotic masses** to those collections of pigment which occur simultaneously in a great number of spots in the body. They are distinguished from infiltrations of pigment in the skin (*nævi materni*), and also from the pigmentation sometimes found round the blood-vessels of the nervous centres, in that in the case of melanotic masses the tissues are destroyed, and secondary growths occur in all the organs, like the most malignant tumours.

Description.—In the records of science we have found but one reliable report of a case of this kind, published by MM. Dubrueil and Lancereaux. We have investigated a similar case, submitted to us by M. Landrieux. Contrary to the generally slow progress of simple melanosis in the horse, in which animal the disease is very common, in man products of this kind generalise with extreme rapidity, and cause death. The progress of the disease is so rapid that it is often difficult to decide if a primary mass has caused secondary infection of the organism, or if the numerous masses result from some general cause. These melanotic masses vary greatly in size from that of a microscopic granule to that of an egg or fist. They are well defined, and at their edges no intermediate zones of tint are found between them and the normal tissues. When they have obtained the size of an almond they are soft at the centre, while the periphery is as firm as the tissue in which they are developed. Nothing is discovered under the microscope in the central softened fluid mass except melanotic granules, the smallest of which are agitated by Brownian movements.

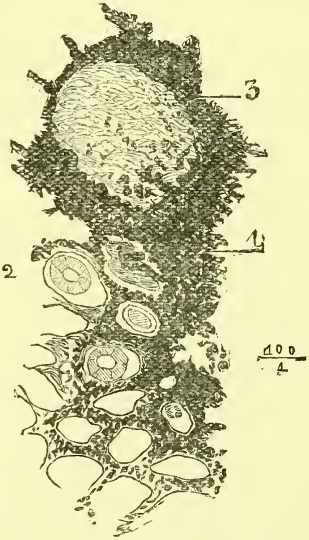

Fig. 177.—Section of Kidney.

1, pigment deposited in the stroma of the organ; 2, uriniferous tube; 3, glomerulus. Magnified 100 diameters.

The microscopical examination of the parts which are still firm is made from sections cut after hardening in alcohol. The constituent elements of the parent tissue are then found to be infiltrated with melanotic granules, without there being any evident new formation of cells. Thus, in the subcutaneous cellular tissue, the connective-tissue cells are seen to be infiltrated with pigment, recalling the pigmented stellate cells of the choroid (vide fig. 40). In the peritoneum, the melanotic granules are primarily deposited in the connective-tissue cells, exactly as in the corium. A similar pigmentation of cells is observed in the trabeculæ of the great omentum, which is non-vascular. Soon, however, the cells are entirely hidden by the accumulation of pigment which is then deposited in the fibrous tissue. The large nodosities are formed by the union of masses originally solitary. In the kidney, the deposit of pigment is seen either in the form of spots or of small black granules. Sections examined under the microscope show that the

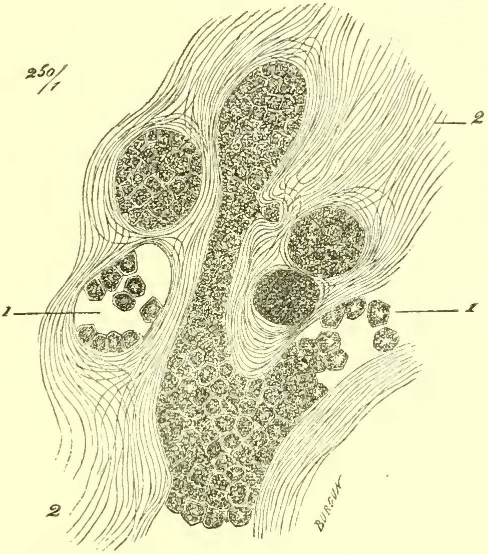

FIG. 178.—EPITHELIAL CELLS OF THE GALACTOPHOROUS ACINI INFILTRATED WITH BLACK PIGMENT.

1, galactophorous cells and acini; 2, interstitial connective tissue. Magnified 250 diameters.

pigment is localised in the cellulo-vascular framework and in the glomeruli; the epithelium of the tubuli remaining intact for a long time (vide fig. 177).

In the case which we examined there were spots, visible to the naked eye, in the nipple; the melanin was deposited in the glandular ducts and acini, but not in the connective tissue. In rather thick sections treated by tartaric acid, the acini of the gland were well seen, some of them were normal and others stained black. With a high power, and in sections made after hardening in alcohol, it could be clearly seen that the melanotic granules were deposited round the nuclei in the protoplasm of the cell (fig. 178). In our own case, and in that reported by MM. Lancereaux and Dubrueil, pigment was found deposited in the muscular fasciculi of the heart. These facts prove beyond doubt that pigment is deposited simultaneously in the connective-tissue cells and epithelial cells, and even in the muscular fasciculi, and that it does not come directly from the colouring matter of the blood. We believe, in fact, that melanotic change is not produced by simple penetration of pigment, but that it is the result of pathological activity of the cells themselves.

This morbid species can only be mistaken for melanotic carcinoma or sarcoma; but from naked-eye appearances alone, simple melanosis may be suspected, if between the black and the healthy tissue no zone is found showing intermediate tints; this is hardly ever wanting in melanotic carcinoma and sarcoma. To be certain that the diagnosis is correct, it is not sufficient to scrape the tumour, nor to examine the elements obtained by dilaceration, but, as we have already said, delicate sections must be cut.

The generalisation of melanotic masses is always very rapid, and death occurs at the end of a few months.

HYDATID CYSTS.

Hydatids are described in the part of this work which treats of general pathology, for they are met with in all organs and tissues. The other human parasites which have a special habitat will be described when treating of the tissues and organs in which they are found. Thus trichinæ will be described in connection with striated muscles, and the trichophyton and microsporon with the skin, etc.

Definition.—Hydatid cysts, which owe their name to the transparent fluid they contain, are essentially caused by the vesicular worms which represent a phase in the development of tænia. In man only two kinds of hydatids are found, the **cysticercus** and the **echinococcus.** The cysticerci are solitary in their cysts, while the echinococci are produced in more or less considerable numbers in a primitive cyst. They proceed from various species of tænia, but most frequently the *Cysticercus cellulosæ* (Rudolphi) belongs to the *Tænia solium.* To understand their place in the zoological series and their mode of production it is necessary first to give a clear description of the tænia.

The **Tænia Solium**, which lives in the small intestine of man, is a riband-shaped, white worm, many yards in length; it is composed of rings the smallest of which are near the head, while the largest are found at the opposite extremity. The head is about the size of a pin's head; on it are four suckers and a small tubercle or proboscis, the base of which is surrounded by twenty-four to twenty-eight hooks, arranged in two series. The entire head is called by the name of *scolex*. The rings situated immediately after the head gradually increase in size as the other extremity is approached. These rings, which may have a diameter of 12 mm., are flat, and each represents a hermaphrodite individual. The orifices of the male and female genital organs are united at a slight eminence, situated at one of the borders of each ring;

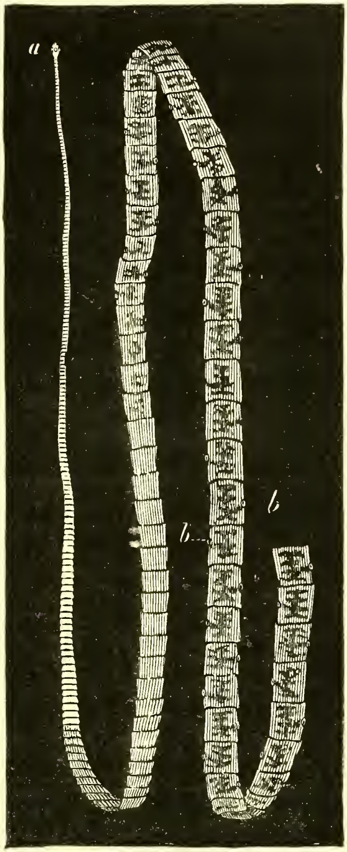

Fig. 179.—Tænia Solium.
a, head or scolex; *b*, rings or proglottides.

these organs are composed of sinuous ducts which represent the uterus and ovaries; the latter being filled with ovules; the male organ consists of a falciform penis and a seminiferous duct. The fecundated egg, in the ripe rings, contains an embryo already provided with six hooklets. The ultimate rings become detached; they are called proglottides or cucurbitini. They are filled with fecundated eggs, and if swallowed by certain animals, pigs for example, the eggs lose their enveloping membranes on reaching the intestine, and the liberated embryo passes through the intestinal walls, to be located in various parts of the organism, where it becomes the cysticercus cellulosæ. The presence of cysticerci in pork constitutes pig measles (*ladrerie*).

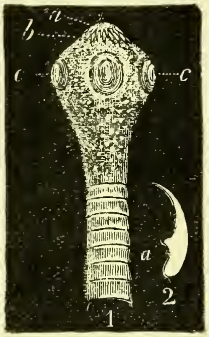

FIG. 180.—HEAD AND NECK OF THE TÆNIA SOLIUM.

a, proboscis; *b*, crown of hooklets; *c*, *c*, suckers; 2, an isolated hooklet; *a*, hinge-like projection by which it is attached to the head of the tænia.

The **Cysticercus cellulosæ**, which is seen very rarely in man, is found in the muscles, pia-mater, and brain, beneath the conjunctiva, in the chambers of the eye, in the pleura, and peritoneum, etc. It is generally encysted. The cyst wall is formed of a membrane of connective tissue supplied with blood-vessels. This membrane is deficient when the cysticercus is located in a natural cavity. On incising the membrane, the cysticercus is found in the form of a round vesicle, from eight to twenty mm. in diameter, filled with a transparent fluid. On its surface is seen a slight depression. On pressing the vesicle, the body, neck, and head of the animal protrude from out of its caudal receptacle (fig. 181). The head is exactly like that of the Tænia; on the neck and body of the animal are folds or rugæ, without any distinct rings, and there are no genital organs. For the cysticercus to attain the perfect development of the tænia it is necessary for it to pass into the intestinal tube of another animal. The tænia solium of man is most frequently derived from the cysticercus contained in pork. The cysticercus cellulosæ is not the only variety found in man, some isolated cases have been reported of the cysticercus of the *Tænia acanthotrias* and of the *Tænia serrata*, etc. If the forementioned cysticerci are rare in man, echinococci are, on the contrary, very common. They bear the same relation to the tænia echinococcus as the cysticercus cellulosæ does to the tænia solium.

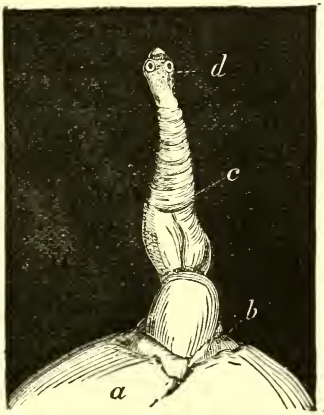

Fig. 181.—Ladric Cysticercus.

a, adventitious cyst; *b*, sac in which the animal becomes invaginated; *c*, body; *d*, head with proboscis, suckers, and double row of hooklets.

The **Tænia echinococcus**, the existence of which is doubtful in man, lives in colonies in the intestine of the dog. It differs from the Tænia solium chiefly by the small number of its rings, of which the third or fourth from the head contain eggs and become detached. On reaching the human intestine, the eggs of this tænia lose their enveloping membrane, and the embryos locate themselves in the serous cavities and in the parenchymatous tissues. They are the point of departure of cysts, which, when fully developed, are composed of an adventitious fibrous membrane, belonging to the organ affected, and of one or more vesicles, which are free or contained one within the other. These transparent, tremulous vesicles, which give to the hand the characteristic sensation known as the hydatid thrill, are spherical, and vary from the size of a nut to that of an orange. They contain a transparent fluid which is not coagulated by heat nor by acids. The membrane of the cyst is gelatinous, transparent, and formed of delicate superimposed leaflets, which may be separated by dissection, and roll up in the same way that elastic membranes do. On microscopical examination, the leaflets appear to be formed of amorphous and still more delicate lamellæ, separated from one another by beautifully distinct parallel lines. The most internal, called the germinal membrane, has attached to its free surface echinococci, which appear to the naked eye as small whitish granules. Some of them become detached and float in the fluid. Within the large vesicles much smaller vesicles of identical structure are often found. The echinococcus is formed of a caudal vesicle, adherent to the germinal membrane, in which is found the head and body of the invaginated animal, just as in the cysticercus.

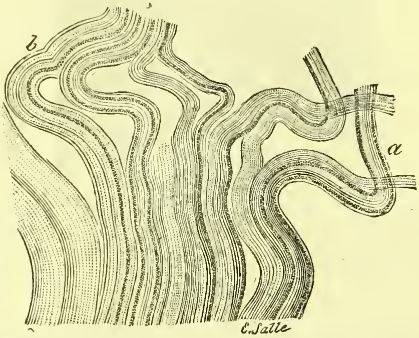

FIG. 182.—DELICATE SECTION OF A PORTION OF THE MEMBRANE OF A HYDATID CYST.

Magnified 200 diameters.

Echinococci vary in diameter from ·1 to ·2 mm. On the head is a proboscis, a double row of hooklets, and four suckers. Scattered over the body of the animal are calcareous plates.

Hydatid vesicles do not always contain echinococci. The germinal membrane may be deficient, or the echinococci may have ceased to live; in the latter case hooklets are found free in the hydatid fluid. This variety of sterile hydatid cyst has been called acephalo-cyst. In certain cases, the wall of the vesicles is very thick, and composed of a large number of superimposed lamellæ, the central cavity being small.

A variety of hydatid cysts, called **multilocular hydatid tumour,** has been recently described by Friedreich, Virchow, Ost, etc. It is characterised by the presence of a large number of very small miliary cysts in a fibrous stroma.[1] Each of these cysts contain one or more hydatid vesicles, inclosing echinococci or hooklets; but even if the latter are not present, the cysts are always characterised by the membrane peculiar to hydatids. There is at first sight a great resemblance between these tumours and colloid carcinoma, with which they are easily confounded; but after microscopic examination, hesitation ceases.

If hydatid cysts remain long in the organism after reaching perfect development, their different constituent parts undergo great modifications. The fluid is absorbed, the echinococci become detached and decomposed, the hydatid membranes collapse and break down into flakes suspended in a thick soup-like fluid which is rich in calcareous salts, and in cysts of the liver, stained of an ochrous or reddish hue from the presence of the colouring matter of the bile. The adventitious membrane—that is to say, the fibrous membrane belonging to the organ in which the hydatid is developed, and which forms its external envelop—becomes thicker, retracts, and often undergoes fatty or calcareous infiltration. In the adventitious fibrous membrane of an old cyst of the liver we have observed spots of osseous tissue containing veritable osseous trabeculæ, medulla, and blood-vessels. We are, however, only aware of this solitary example, for generally in very old hydatid cysts the adventitious membrane undergoes simple petrifaction, a carapace being formed composed of superimposed calcareous lamellæ united by fibrous tissue.

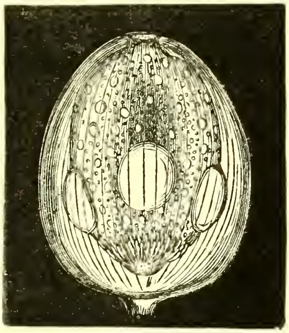

Fig. 183.—Invaginated Echinococcus, detached from the Mother-hydatid.

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[1] These tumours are extremely rare in France; we have had but one opportunity of studying them in specimens brought us by M. Carrière, and which he made the subject of his inaugural thesis in 1868.

The relation of vesicular forms with tænia was established by the experiments of Van Beneden, Küchenmeister, Leuckart, etc. In the last edition of the excellent treatise on entozoa by C. Davaine, 1877, will be found an examination of all the known facts regarding the parasites of man and animals.

PART II.

DISEASES OF THE TISSUES.

CHAPTER I.

LESIONS OF THE BONES.

Lesions of the bones are important, not only on account of their number and variety, but because the ease with which they are produced, their precise development, and their easily comprehended evolution guide pathologists in their researches on other tissues, and suggest to them general ideas regarding pathological histology. These considerations have induced us to commence the study of lesions of the various tissues of the organism by those of osseous tissue.

The development of osseous tissue is typical, and enables us to understand most of the pathological phenomena which occur in bone. As we have already seen, osseous tissue does not result from the direct transformation of cartilaginous tissue, for in its formation the cellular elements of the cartilage become free and give origin to embryonic medulla, the cells of which are subsequently changed into bone cells. Those embryonic cells which do not become bone corpuscles undergo changes which differentiate them from the original type; some preserve their primitive characters, while others diverge widely; thus some become fat cells; some aid in the formation of a true connective tissue, which may be observed round the blood-vessels of a certain calibre, and between the fat cells of the medullary spaces or the canals of the long bones; others again do not divide while their nuclei multiply, thus forming the giant-cells of bone medulla; later, these become dry and flattened in the form of lamellæ in which nuclei are included (myéloplaxes).

Almost all the pathological phenomena observed in bones have their starting-point in the cells of the embryonic medulla, or in those cells which have undergone some one of the modifications indicated above. The bones of young persons, or those which in the adult contain fœtal medulla, as the sternum or vertebræ, are particularly exposed to both nutritive and formative pathological changes. Different parts of the same bone are however not equally subject to the same disease; the most recently formed, that is to say, the superficial or subperiosteal parts, or the bony extremities, particularly when still growing, are those which are most easily affected. Diseases of the osseous system are much more varied and much more frequent than the classical descriptions would lead one to infer; this is owing to the fact that surgeons only investigate bone lesions when they possess some great clinical interest, and also that the skeleton is very rarely examined in post-mortem examinations.

I. Congestion and Hæmorrhage of Bones.

Congestion of bone is recognised by the red appearance of the marrow. To appreciate this change the normal colour of marrow in various bones, and at different ages, must be known. The medulla is red in the sternum, and in the bodies of the vertebræ, and also in those parts of the bone which are undergoing development. In young subjects the epiphyses, adjacent to the cartilage of ossification, show a condition of physiological congestion, while in parts long formed the medulla is fatty and has the yellow tint and translucent appearance of adipose tissue. In more advanced age, the medulla of the vertebræ and sternum loses its colour and becomes paler. The red colour of marrow is not always related to congestion. To ascertain its cause, however, histological examination is necessary. Sections should be cut after maceration in a ·5 per 100 solution of chromic acid, or in a saturated solution of picric acid.[1] In such preparations, preserved in glycerine, it will be seen that bones, containing red-coloured marrow in the fresh state, do not owe this appearance solely to the fact of the capillaries being dilated and full of red blood corpuscles, for congestion is frequently accompanied by rapid proliferation of the medulla cells, and more or less complete absorption of the fat. Diffuse hæmorrhages may sometimes occur, and red blood corpuscles are then found mixed with the medulla cells. The extravasated red corpuscles slowly undergo considerable changes; their colouring matter is set free and infiltrates the elements which were hitherto colourless, or they themselves may be absorbed by the young medulla cells in which they may be found intact; in other cases, the medulla cells only show granules of hæmatoidin or a slight yellow tint. Thus it is seen that in bones the redness of the medulla may be due to congestion, to hæmorrhage, or to staining of the medullary elements with hæmoglobin. It may also be due to newly formed blood-vessels, in which case it is no longer one of simple congestion.

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[1] To obtain good preparations the piece to be examined should be small and immersed in a large quantity of the solution; otherwise the amount of acid is insufficient to dissolve out the calcareous salts and to give the bone the consistency required. Picric acid is preferable to chromic acid, for it never crystallises, and preserves the blood corpuscles better; also preparations so obtained stain well with carmine. Chromic acid may, however, be used, provided that purpurin be employed as the staining agent.

Simple or complicated congestion of the medulla is met with in a great number of conditions, such as ostitis, caries, various tumours, rachitis, and osteomalacia; it is easily produced, for the medullary blood-vessels are not supported by a solid framework. It is seen also in purely physiological conditions related to a formative movement, such as ossification, and it often accompanies the development of new blood-vessels, at the same time that it causes extravasations of the red blood corpuscles into the medullary parenchyma.

Hæmorrhage into bone is frequent in the spongy tissue and under the periosteum, owing to the fact that in these parts the blood-vessels are not solidly supported; it may be observed not only as a consequence of traumatism, contusions, wounds, and fractures, but whenever there are marked changes in the walls of the capillaries, such as are observed in inflammation, and active new formations (*vide* p. 92). The walls of the capillaries, composed at such times of embryonic cells, become so soft that the blood corpuscles easily pass through them, and are extravasated into the medullary parenchyma. In a third category of facts, osseous apoplexy is related to one of those general diseases which cause hæmorrhages, such as cachexia, purpura, leucocythæmia, etc. Whenever hæmorrhagic foci are found in the viscera, similar foci may almost always be found in the epiphyses of the bones, or under the periosteum.

II. Ostitis.

When a bone is submitted to some simple cause of irritation, such as denudation, a wound, the presence of a foreign body, etc., it undergoes certain modifications which serve to establish the anatomical definition of ostitis. The irritation causes excessive functional activity of the osseous cellular elements, and the lesions which follow are directly consequent. These lesions do not differ essentially from those produced in other tissues by similar causes, being, in fact, those of inflammation.

Experimental production of ostitis.—If in an animal the surface of a bone be denuded and the wound kept open, an enlargement of the Haversian canals by absorption of the osseous substance is observed at the end of a few days, while under the periosteum, at the periphery of the denuded surface, a layer of newly formed bone is already perceived. This simple experiment shows that irritation simultaneously causes both absorption and exuberant production of osseous tissue. How is it that the same cause produces results so different? This is our first subject of study, for here may be found almost the whole histological history of ostitis.

The first phenomenon observed in a bone submitted to artificial irritation is the formation of embryonic cells in the medullary spaces, the Haversian canals, and under the periosteum. These cells resemble those which fill the primitive medullary spaces during the development of bone from cartilage, or those found under the periosteum when bone increases rapidly in thickness. They are derived from the various cells composing the medulla (*vide* p. 21). Hence we see that irritation brings bone back to an embryonic condition, and here we find an application of the general law governing the irritation of all tissues.

The phenomena resulting from the production of embryonic tissue in the medullary spaces and under the periosteum are the following. A. *The enlargement of the Haversian canals and the medullary spaces by absorption of the osseous tissue which limits them.* B. *The formation of new osseous trabeculæ.* It is advisable to study each of these phenomena separately, and then to ascertain what relation there is between them.

A. **The enlargement of the Haversian canals** may be easily seen in preparations made as described on page 326 (see footnote). The osseous lamellæ are then observed to be eroded so as to form notches filled with embryonic cells (Howship's lacunæ, fig. 185 *b*, *c*). On the edge of these notches the bone corpuscles open and permit the cells they contain to escape, and mixing with those filling the medullary spaces they become indistinguishable from them. Little by little the osseous lamellæ disappear in places, and the Haversian canals communicating, form large irregular spaces filled with embryonic medulla.

The cause of the absorption of the osseous substance is still veiled in obscurity, though many hypotheses have been put forth in explanation. Billroth, having remarked that the serous pus of chronic bone abscesses contains lactic acid or acid phosphates, was led to think that the solution of the bone depended on the presence of these substances. To reverse this opinion, it is enough to show that, as may be seen in necrosis, pus has only a feeble action on the fragments of dead bone which form sequestra. Rindfleisch thought that absorption of bone was preceded by its mucoid degeneration. It is true that in some preparations a zone clearer than the adjacent osseous tissue may be observed at the edges of trabeculæ which are undergoing absorption; but it seems to us that this zone is due to the fact that the section has been cut obliquely. Virchow is of opinion that the bone corpuscles enlarge, undergo change, and bring about solution of all the osseous substance which corresponds to the cartilarge capsule from which the bone corpuscle and the tissue surrounding it were originally developed, and on this interpretation he founds his theory of cellular territory. This interpretation cannot be accepted, for it is now known that bone corpuscles do not proceed directly from cartilage capsules. O. Weber and Volkmann consider that absorption of the osseous substance depends upon fatty degeneration of the bone corpuscles; this error arose from their confounding caries with rarefying ostitis. It will be shown later that true caries is the only disease in which granulo-fatty de-

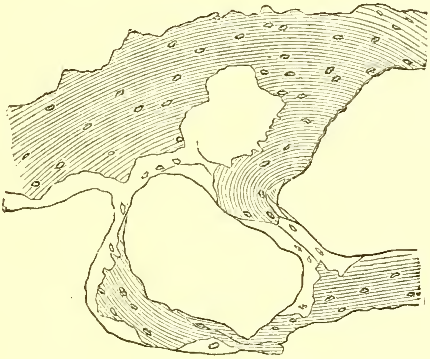

FIG. 184.—RAREFYING OSTITIS OF THE PHALANX OF THE BIG TOE IN A CASE OF PERFORATING ULCER OF THE FOOT.

Section cut after maceration in a ·5 per 100 solution of chromic acid. A clear zone is observed at the edges of the lacunæ; but in the upper part of the preparation, where the section has been cut perpendicularly to the surface undergoing absorption, this zone does not exist.

generation of the bone corpuscles is observed, and that in this disease the osseous trabeculæ, in which the change has taken place, die without being necessarily absorbed. The bone corpuscles found at the edges of the trabeculæ, which are notched by the progress of ostitis, are often in a condition of perfect integrity. Sometimes the cell within is slightly larger and more defined than usual, but signs of proliferation are rarely present, and the cells never contain fatty granules.

It is thus seen that it is very difficult to form a positive opinion as to the cause of the absorption of bone in ostitis. Though, in acute ostitis, osseous cavities are sometimes found containing one large cell or many cells resulting from multiplication of the primitive cell, so that the enlarged cavity may open into a medullary space, yet this is, nevertheless, not the usual mode of the absorption of osseous trabeculæ; more often the lacunæ produced by loss of substance are seen in sections to have a rounded notched appearance (fig. 185), and seem to be formed by cellulo-vascular buds which spring from the growing medulla. Kölliker, who has seen the same notches produced in plates of ivory inserted in bone, maintains that absorption is due to the activity of certain cells of the medulla, the mother-cells or myeloplaxes, to which he has given the name of *osteophagi* or *ostoclasts*. The rôle attributed to these cells seems to us to be hypothetical, for they are found at the edges of osseous trabeculæ in process of growth, as well as near those which are undergoing absorption in inflamed bone. The absorption of the osseous substance in ostitis seems to us to be more closely related to the action of the vascular buds of the medulla, which act upon the osseous trabeculæ in the same way as medullary buds do in physiological ossification, or as aneurisms of the aorta on the sternum. The absorption of the osseous trabeculæ cannot be attributed to the action of pus; we have ourselves examined necrosed bones which had lain for a number of years in purulent foci, the pus of which was caseous, without finding any erosion of the superficial osseous lamellæ (*vide* NECROSIS).

The formation of new osseous trabeculæ takes place by the agency of the embryonic cells which have been produced in the first stage of inflammation. Irritation first prepares the materials of ossification, but these are not utilised in the development of new osseous trabeculæ till the irritation has lost its original intensity. Thus new osseous tissue is not produced at the spots where inflammation is acute, but in the parts adjacent to the inflammatory focus. The subperiosteal medulla possesses in the highest degree the property of producing bone, as has been well demonstrated by Ollier's experiments. The rapidity with which osseous tissue when irritated is formed beneath the periosteum is truly prodigious. The mode does not differ from the physiological type (*vide* p. 24). For new osseous tissue to be rapidly developed on the surface of a denuded bone, it is not necessary that it should be covered with periosteum, though the preservation of the periosteum, and particularly of the blood-vessels which pass from its under surface into the Haversian canals, greatly favours the formative process. It is not only, moreover, on the surface of inflamed bones that osseous tissue is produced ; in fact, when inflammation ceases, the anfractuous cavities which have been hollowed in the bone are soon filled up by new osseous layers which are developed in exactly the same way as on the surface of the bone. The medullary canal itself may become the seat of new osseous growths, if the central medulla has been irritated. These facts show clearly what is the relation, in ostitis, between rarefaction and formation of osseous tissue, that is to say between rarefying and formative ostitis. In the inflammatory rarefaction of bones, the materials of re-edification are prepared ready to be used by the organism the moment that the irritation ceases : an application of the laws formulated on page 116. If the irritation persists with all its original intensity, granulations and pus are produced on the surface of the bone. The granulations spring directly from the medulla contained in the enlarged medullary cavities, and show, as Troja observed, that the osseous tissue comprised between several canals has been absorbed. This absorption continuing, all the denuded surface may be covered by a soft, granular, and highly vascular layer.

From this general description of ostitis we pass on to the study of its several varieties. We shall consider acute and chronic ostitis together, for the distinction between them is more interesting clinically than pathologically; neither can we distinguish between periostitis and osteomyelitis, for periostitis is, in fact, simply superficial ostitis, and histologically considered ostitis is essentially characterised by phenomena which occur in the medulla ; so that every ostitis is, in fact, an osteomyelitis. We shall treat separately, **simple ostitis, rarefying ostitis, formative ostitis,** and **diffuse phlegmonous ostitis.** Caseous ostitis, being almost always related to caries, tubercle, or gummata of the bone, we shall not treat separately.

I. Simple ostitis.—The phenomena of simple ostitis may be seen as the result of severe traumatism, contusions, compound fracture, etc., if necrosis does not take place. The most perfect example of it is seen in the extremity of a bone six or eight days after amputation. The medulla under the periosteum, in the Haversian canals, and a portion of that in the central canal, becomes embryonic ; the periosteum is congested, slightly tumefied, infiltrated with serum, and easily detached from the bone, from which it is separated by a layer of round or angular cells resembling those of embryonic medulla; the Haversian canals enlarge and are filled with similar elements, and opening into one another form an anfractuous lacunar system. The canals, which are divided in sections of the bone, are seen with the unaided eye as red points, or as openings from which small fleshy granulations project. At the same time new osseous trabeculæ are seen to be formed under the periosteum, from the embryonic medulla which has been produced by the irritative process.

The new formation of bone never begins at the point where the irritation is most intense, that is to say, on the surface of the divided bone, nor in the midst of the parts which are suppurating, but at a certain distance beyond. If the stump is conical and the bone projects, traces of new ossification are found, not at the level of the wound, but a little higher up, and new osseous trabeculæ are produced on the surface of the bone. This subperiosteal osseous formation, coincident with absorption of the old bone, must not be attributed to any osteogenic property of the periosteum, for it is, in fact, the medulla-elements, developed by an irritative process under the periosteum and in the Haversian canals, which, as the irritation subsides, concur in the formation of new bone. When cicatrisation of the wound is complete, osseous tissue of new formation is produced in the formerly enlarged Haversian canals and in the medullary canal, and when cure is obtained, the medullary canal is obliterated by an osseous plug, and the extremity of the stump is formed of a round mass of compact osseous tissue, covered with a new periosteum. Similar phenomena occur in every case of simple ostitis, provided necrosis does not take place.

It is thus seen that simple ostitis, taking a natural course towards resolution, is rarefying at the beginning and condensing at the end ; we have therefore no more reason to call inflammation of the bone of a suppurating stump rarefying ostitis, than to give it the name of condensing ostitis, when the stump has cicatrised. Hence it is seen how necessary is the study of the pathological evolution of lesions, in order to arrive at a rational nomenclature.

II. **Rarefying ostitis.**—When in inflammation of the bone absorption of the osseous substance is the dominant phenomenon, and the Haversian canals by continually enlarging eventually bring about the entire disappearance of the bone, we call the ostitis rarefying. This variety of ostitis is remarkable by the absence of any attempt at new ossification. The focus of inflammation, lined with large granulations, is generally in communication with the external air and secretes pus.

Thus defined, rarefying ostitis is an uncommon disease. It may be observed in the small bones of the upper and lower extremities, or as the result of traumatism, or of a continuous irritation, such as perforating ulcer of the foot. In the latter disease particularly, one or more phalanges may entirely disappear without necrosis, though necrosis is sometimes met with in perforating

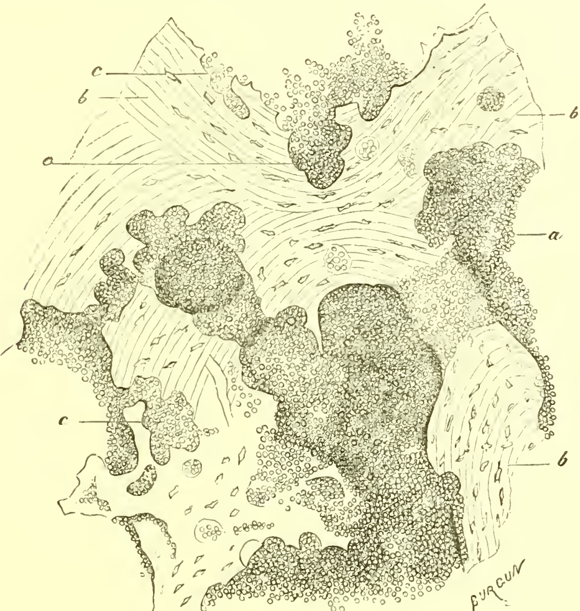

Fig. 185.—Acute or Fungoid Rarefying Ostitis.

a, embryonic medullary tissue; the osseous lamellæ, *b*, are notched in an irregular and festooned manner (Howship's lacunæ) by the formation of medullary cells, as at *c*. Section made from a bone decalcified by the action of chromic acid. Magnified 100 diameters.

ulcer. The diseased bone forms the base of a suppurating and more or less sinuous wound, lined with granulations. These granulations, which are large, succulent, red or greyish in colour, are continuous, at the level of the bone, with an inflammatory tissue which extends into the enlarged osseous cavities. This inflammatory tissue has all the characters of bone granulations (p. 93 and p. 111), and resembles that of certain sarcomata of bone, but is distinguished from them by the fact that in ostitis suppuration is an initial phenomenon, and is continuous during the whole time absorption of the bone is proceeding; ostitis is, moreover, capable of undergoing spontaneous cure. The inflammatory tissue at the base of the granulations may, sometimes by spreading into the substance of the bone, isolate portions of osseous tissue, which thus form living sequestra possessed of blood-vessels and embryonic medulla, and which consequently are capable of being absorbed equally as well as the osseous tissue left *in situ*. Fig. 185 is drawn from a preparation of one of these sequestra. Living sequestra must be distinguished from the dead sequestra found in necrosis, and which are destitute of blood-vessels.

The absorption of osseous tissue in rarefying ostitis occurs in exactly the same way as in simple ostitis; the process is only more intense and continuous. Starting from the focus of suppuration, it extends towards the two extremities of the diseased bone. When an entire bone—a phalanx, for example—is entirely absorbed, acute arthritis is produced at the same time. Not a trace is then left of the old bone, nor of the cartilage, excepting sometimes a thin, opaque, friable lamella, formed by the calcified layer of the diarthrodal cartilage, which is easily recognised under the microscope. On examining this lamella in glycerine with a power magnifying 150 diameters, a granular ground substance is noticed containing large, round, granular, and dark corpuscles, which are the representatives of the cartilage capsules infiltrated with calcareous salts.

III. **Formative ostitis.**—Whenever ostitis ends in recovery it determines a new formation of bone. This new formation is sometimes effected before the cessation of the ostitis. Sometimes ossification does not exceed the limits of the old bone, in which case the ostitis does not then merit the name of formative; in other cases, on the contrary, the new formation is exuberant, and either exceeds the original limits of the bone, or causes the osseous tissue to become more dense. The disease is then called hyperostosis, exostosis, enostosis, or condensing ostitis. All these varieties are included among formative ostitis; nevertheless it must not be concluded that all osseous growths are related to ostitis (on this subject see OSTEOMA, p. 225). The subacute form of the inflammatory process and the length of time it lasts are the usual causes of formative ostitis. Thus it is particularly observed in deeply seated and chronic bone abscesses, in necrosis, and in syphilis of the bones. These diseases are, as is well known, characterised by the slowness of their progress.

We do not propose to include callus in our description of formative ostitis, for owing to the importance of the subject it will be considered separately. New bony growths may be developed on the surface of the bone under the periosteum, or in the substance of the bone itself, or in the central medulla.

a. **Osteophytes.**—In subacute ostitis of long duration, irregular osseous masses, called osteophytes, are found on the surface of the bone. The trabeculæ and blood-vessels of these new growths have a direction at right angles to those of the parent bone, so that it is extremely easy to distinguish one from the other. On examining the section of a long bone covered with osteophytes, the Haversian canals of the bone are seen to be divided transversely, while most of the canals of the osteophytes are divided longitudinally. The direction of the Haversian canals is subordinate to that of the blood-vessels, and the latter are derived either from the osteoperiosteal vessels, or from buds springing from the Haversian canals on the surface of the parent bone; the new osseous layers are, as in the physiological process of ossification, formed from the embryonic elements of these buds and deposited round the blood-

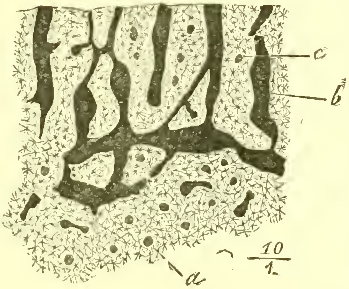

FIG. 186.—PARENCHYMATOUS EXOSTOSIS OF THE TIBIA CUT ACROSS PERPENDICULARLY TO THE AXIS OF THE BONE.

a, Haversian canals of the parent bone cut across in a transverse direction; *b*, Haversian canals of the exostosis, the general direction of which is seen to be perpendicular to those of the old bone. Magnified 10 diameters.

vessels, whence it results that in the new growth the Haversian canals and systems are perpendicular to the surface of the bone on which they are developed.

b. **Eburnation.**—In the body of the bone formative ostitis causes condensation or thickening (condensing ostitis, bony sclerosis, eburnation.) This is generally preceded by inflammatory rarefaction, traces of which may be easily discovered with the microscope. If the embryonic cells contained in the notched and anfractuous cavities which are produced by ostitis cease to be submitted to intense irritation, they aid in the formation of new osseous layers which fill up the irregular festooned spaces. Thus the characteristic border of rarefying ostitis is seen distinctly in bones which have undergone subsequent eburnation. If the inflammatory action continues for several years in the same bone, as, for example, in necrosis or deeply seated abscesses, there are from time to time accesses of acute inflammation, and the bone attains a great size, double or triple that of the normal. The tissue is then extremely irregular, and appears to have been reconstructed many times. The lamellar systems are arranged in the most unexpected manner, and the accidental forms of such a pathological process can be better imagined than described. Eburnation of the osseous tissue produces, not only narrowing of the Haversian canals, but sometimes their complete obliteration (fig. 191); necrosis then occurs from the arrest of capillary circulation in the bone.

c. **Ossification of the central medulla.**—Formative ostitis is rare in the medullary canal. Troja, Ténon, Broca, Ollier, etc., have reported cases of ossification of the central medulla in consequence of ostitis, and we ourselves communicated to the Société de Biologie a case in which a new piece of bone was formed in the interior of the medullary canal of a necrosed bone; as we have already shown in amputations followed by recovery, the extremity of the medullary canal is always closed by a plug of compact bone of varying thickness.

IV. **Diffuse phlegmonous ostitis.**—This disease is called *osteomyelitis* (Chassaignac), *phlegmonous periostitis* (Giraldés), *epiphysial ostitis*, according to the views of the author as to the seat of the lesion. We are of opinion that it consists essentially in diffuse suppurative inflammation which may be seated in every part of the bone, namely under the periosteum, in the superficial layers, in the substance of the bone itself, or in the central medulla. As it occurs particularly in young children, and as growth of the bone takes place under the periosteum and near the epiphyses, the physiological activity of these parts is favourable to more intense inflammation than the rest of the bone.

The primary and dominant phenomenon of the disease consists in the rapid formation of pus, so that on incising the periosteum after the lapse of twenty-four to forty-eight hours a purulent focus is opened (Louvet). In these cases of rapid and extensive suppuration the entire bone may become necrosed, detached from its epiphyses and periosteum, and be contained in an enormous abscess. Purulent infiltration of the cancellous tissue of the extremities

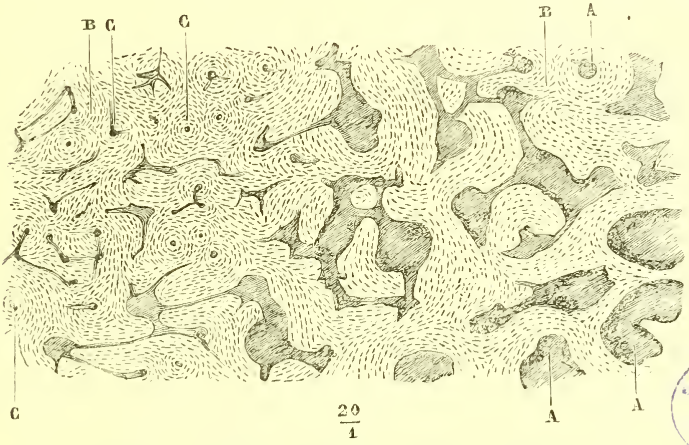

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Fig. 187.—Syphilitic Sclerosis of the Os Frontis.

A A, medullary spaces of the diploe; C C, the same spaces considerably retracted; B, osseous substance.

and of the medullary tissue may then be observed; and it is easily understood how pus, accumulating within the rigid bony walls of the Haversian canals, may compress the blood-vessels, completely arrest the circulation, and cause necrosis. It is essentially a suppurative inflammation, that is to say, inflammation in which pus is the principal product. There is generally in these cases no rarefaction of the osseous tissue, and the necrosed bone presents the same appearance as it does after maceration in water. It is rare for the suppurative inflammation to be so intense and extensive; it may be limited to the neighbourhood of an epiphysis, in which case an abscess is formed on the surface of the bone, on opening which a series of anatomical phenomena are observed, varying according to circumstances. In the least severe cases, the inflammation being superficial, the same lesions occur as in simple ostitis after denudation of the bone, that is to say, rarefaction of the osseous tissue followed by condensation. But the superficial layers of the bone are often infiltrated with pus, in which case partial necrosis may occur. In another series of cases the suppurative inflammation having invaded the medullary canal, or the areolæ of the cancellous tissue, holes are very slowly, and by a process still hidden in obscurity, drilled, as it were, in the substance of the diaphysis or near the epiphyses, by means of which the abscess is drained. In these cases the inflammation is acute at the centre of the bone and almost nil at the periphery, though it persists in a subacute form on the surface as long as there is acute inflammation at the centre. In consequence of this superficial inflammation layers of new bone are, by a process of formative ostitis, deposited under the periosteum, and these being superimposed greatly increase the diameter of the bone. Even when suppurative ostitis is limited, partial necrosis is a very common consequence.

III. Necrosis.

With the majority of authors, we give the name of necrosis to mortification of bone resulting from traumatism or ostitis. Necrosis is caused by an arrest of circulation, generally related to compression of the blood-vessels in the Haversian canals, either by pus or by new osseous growths. When ready for elimination the necrosed bone is called a **sequestrum.** French surgeons distinguish the sequestra of necrosis from those of caries; when treating of caries it will be observed that we consider the distinction legitimate, not only on account of naked-eye appearances, but chiefly by reason of the mode of formation of the sequestrum, as revealed by the microscope. At present, necrosis properly so called will only be considered. In compound comminuted fracture the detached fragments of bone are called splinters. They are either removed by the surgeon or eliminated by suppuration, and are unimportant; not so however the secondary mortification of the bone consequent on inflammation. These cases of necrosis are similar to those which are sometimes seen in a stump after amputation, if there is acute inflammation at the end of the bone or if it projects externally. It is difficult in fact to understand, *à priori*, why after division a thin layer of bone is not always necrosed. After the bone has been sawn through, hæmorrhage is arrested as soon as the blood coagulates in the small divided blood-vessels; the bone cells being deprived of their ordinary means of nutrition, it must be supposed, if they live till circulation is re-established, either that they can for a time exist without nutrition, or that nutritive fluids reach them by another route, for instance, by the surface of the bone being bathed in the plasma of the wound. If the stump is conical, and the surface of the bone in contact with the dressings or the external air, a small part of the bone is generally necrosed. When necrosis results from acute inflammation of the stump, it is caused in a different way. Pus is produced, not only in the soft parts, but in the bone itself, under the periosteum and in the Haversian canals; the blood-vessels contained in these canals are therefore compressed, circulation is arrested, and necrosis results. In the case of wounds with denudation of the bone the conditions are the same as those in a divided bone.

Separation and elimination of the sequestrum.—Whether necrosis results from traumatism, suppurative ostitis, or formative ostitis in which the Haversian canals have undergone obliteration (p. 337), the phenomena of the separation and elimination of the sequestrum are as follows. The necrosed bone, acting as an irritating foreign body, occasions rarefying ostitis around itself, and is soon surrounded with granulations. The adjacent Haversian canals enlarge by proliferation of their medulla, and by absorption of their osseous lamellæ; this process of absorption continuing, the living osseous trabeculæ and those in which the blood-vessels are obliterated are both destroyed, and the canals communicate. The disappearance of the trabeculæ completely isolates the sequestrum in the midst of a granulating medulla. Owing to this process the surface of the sequestrum is not smooth, but furrowed by tortuous depressions, corresponding to the medullary buds of new formation. The method of elimination differs according to the situation of the sequestrum. If located at the periphery of the bone, or under the periosteum, or at the extremity of a divided bone, it is soon isolated in the midst of pus; if it is on the surface of a large bone, or is the result of amputation or denudation of bone, the necrosed part is also eliminated without difficulty; if there is no wound opening externally, a deeply seated abscess is formed, and if this be opened spontaneously or with the knife, the sequestrum which is completely detached may be discharged with the pus; but if the abscess communicates with the external surface by a fistulous opening, the surgeon is able to explore the position of the sequestrum and to perform any operation necessary for its extraction. But if an entire bone, or a large portion of the diaphysis of a long bone, be necrosed, the subperiosteal medulla proliferates, becomes embryonic, and produces new osseous tissue under the periosteum and even beyond it. The new layers of bone slowly become thicker, so that the old necrosed bone is surrounded by new osseous tissue. In this case the extraction of the sequestrum is difficult, and it may remain included for years; the sequestrum is then said to be invaginated. An invaginated sequestrum is never in direct contact with the bone which surrounds it; the latter is lined internally with a layer of granulations, which constantly secrete pus and separate the dead from the living bone. When the pus is not easily drained away by means of fistulous fenestræ, it remains *in situ*, dries, and undergoes caseous degeneration.

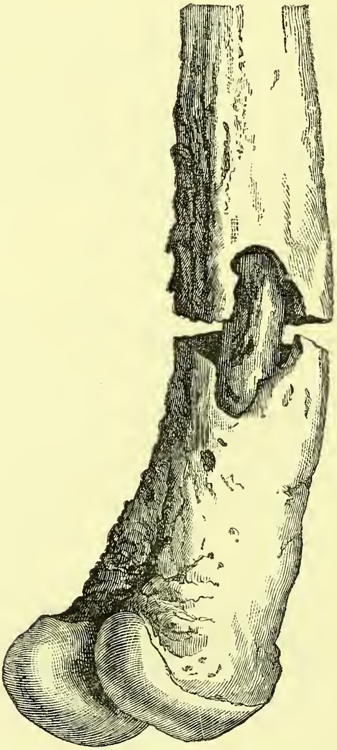

Fig. 188.—Invaginated Sequestrum of the Femur with considerable Subperiosteal Bony Growth.
From the 'Pathological Surgery' of Nélaton.

Action of pus on sequestra.—It is admitted by some that a sequestrum may be absorbed and slowly disappear by the action of pus. This opinion is based upon the fact that inequalities and depressions are seen on the surface of necrosed bone. We are unable, however, to adopt this view, for if sequestra which have remained long in the midst of pus be examined with care, in some of them the surface will certainly be found to be smooth. On microscopically examining a section of such a bone, with a low power, the peripheral osseous lamellæ which normally encircle long bones will be recognised. We have frequently ascertained this to be the case in many old sequestra, one of which had remained thirty years in the midst of pus, and in which, at certain points, we still found the peripheral layers of the old bone. From this we conclude that the solvent power of pus is very limited, if it exists at all. The researches of Billroth and Kölliker have, however, proved that necrosed bone, and even wedges of ivory, may be partially absorbed; but the absorption should not be attributed to the action of pus, for, as we have already pointed out with regard to rarefying ostitis, it is the result of the action of the cellulo-vascular buds of the inflamed medulla.[1]

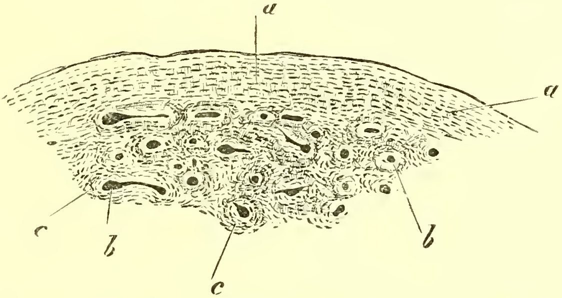

Fig. 189.—Transverse Section of the Sequestrum of a Humerus which had been for Thirty Years in the midst of Pus.

The figure only shows a portion of the surface of the bone where the peripheral lamellæ, *a*, are preserved; *b*, Haversian canals; *c*, Haversian systems. Magnified 20 diameters.

Microscopic appearances of sequestra.—Sequestra and the living bone which contains them have very different appearances according to the progress and cause of the necrosis. Thus in acute suppurative ostitis, sequestra are found presenting the normal structure of bone or the lesions of rarefying ostitis; in chronic ostitis, such as that caused by syphilis or phosphorus-poisoning, the necrosed bone shows special lesions. In syphilitic necrosis, so common in the bones of the skull, the sequestrum corresponds exactly to a certain portion of the bone; it has the same thickness and the same surfaces. The latter, however, have generally a roughened appearance from small losses of substance, so that it might be thought, at first sight, there was some rarefaction of the bone; but on making a section through the sequestrum, it will be seen that, on the contrary, the diploe is transformed into compact tissue. Such a sequestrum is not invaginated as in the long bones, but around it new bone is thrown out which overlaps the edges and holds it, in the same way that a watch-glass is held. In most cases of syphilis, formative ostitis extends over a large

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[1] Very beautiful preparations of osseous tissue may be made from sequestra, for the fatty substances and cellular elements have been completely destroyed by the prolonged maceration in pus.

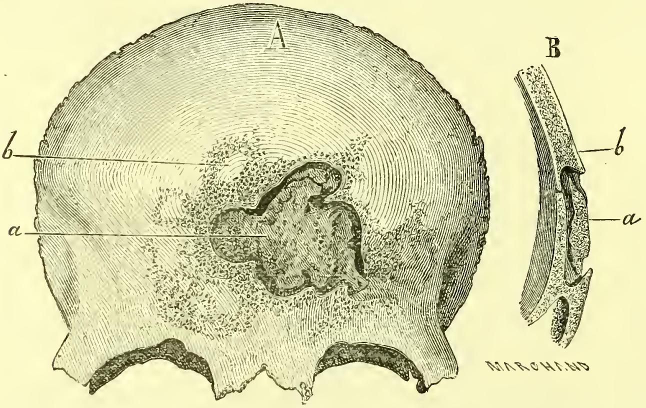

FIG. 190.—SYPHILITIC NECROSIS OF THE OS FRONTIS WITH PRODUCTIVE OSTITIS.
A, os frontis; *a*, sequestrum; *b*, circinate and eburnated bony growths developed under the pericranium; B, longitudinal section through the sequestrum *a*, and the part of the living bone *b*, in which it is lodged.

area and forms small, flat, often circinate hyperostoses (vide *b*, fig. 190). Examined under the microscope the medullary cavities of the diploe are seen to be replaced by very narrow channels, and in good preparations this change is seen to have been caused by a formation of osseous tissue, which, deposited layer by layer on the internal surface of the canals, has narrowed them. These osseous layers are often so arranged that the lumen of the canal is not in the centre of the primitive cavity. By continuation of the process the canal may be entirely obliterated, so that, instead of a canal in the centre of concentric layers, there is osseous substance containing one or more bone corpuscles (fig. 191). Near the sequestrum there is often more or less extensive sclerosis of the diploe of the living bone, which may sometimes even be general. In a section cut at right angles to the surface, the whole process of condensation may be followed at certain points (*vide* fig. 187), just as we described it when considering formative ostitis. In necrosis of the maxilla, found in workers in phosphorus, the sequestra are heavy, eburnated, and often have superficial spongy osteophytes, which are easily detached. In that part of the sequestrum which belongs to the old bone, the lesions of condensing ostitis may be recognised. This condensation of the osseous tissue and the production of osteophytes show in a distinct manner that necrosis was preceded by slow formative ostitis.

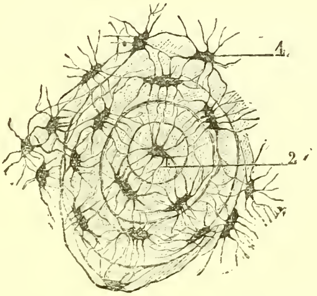

Fig. 191.—Section of a Sequestrum in Syphilitic Necrosis. Part of the Preceding Figure Enlarged.

This figure represents a Haversian canal obliterated by successive layers of bone corpuscles, and ground substance arranged in regular lamellæ. 1. Bone corpuscles; 2. Centre of the Haversian canal. Magnified 300 diameters.

IV. Caries.

The disease of the bones called caries is defined in a very vague manner by pathologists. Surgeons call caries every suppuration of osseous tissue accompanied with great friability. Their diagnosis is made by introducing a probe by a fistula into the substance of the bone, and breaking down a certain number of the osseous lamellæ, in doing which a crackling noise is produced and the hand given a peculiar sensation. Pathologists, however, do not agree regarding the anatomical characters of the disease. German pathologists use the word caries to signify rarefaction of bone; according to Virchow, the changes in a bone after amputation, and the cavities which lodge syphilitic gummata of the skull, are both equally due to caries. Billroth considers the name caries as absolutely synonymous with chronic ostitis, with 'melting of the bone,' and he describes many forms of caries, according as it is located in the superficial or deep layers of bone, and according to the appearance of the diseased parts, which may be sometimes vascular—*fungoid caries*—at others quite bloodless—*atonic, torpid, or caseous caries*; he also admits a *necrotic caries*. Thus considered, caries includes a large part of the diseases of bones. We consider that the various lesions described by different authors in caries are all the result of one initial lesion, which consists in *fatty change destructive of the cells contained in the lacunæ.* Our researches have also led us to recognise two distinct periods in caries: in the first, *the bone cells undergo fatty degeneration without there being previously the least sign of inflammation*; in the second, *the osseous trabeculæ, killed by the death of their cellullar elements, form so many small foreign bodies which determine suppurative inflammation around themselves.* This second period, in which ostitis takes on special characters according to the cause which produced it, is that which has alone been described by other observers.

The initial lesions and first period of caries.—Caries generally occurs in short bones and in the extremities of long bones; among short bones the bones of the feet are most frequently affected. It is almost always accompanied, preceded, or followed by chronic disease of the joints—white swelling. The epiphysis of a joint, recently affected with white swelling, is formed of extremely fine trabeculæ in the midst of a fatty medulla. To separate the trabeculæ and distinctly see the delicate reticulum they form, a current of water should be directed on the spongy tissue; they may then be removed with the forceps, and examined under the microscope. It is then seen that they are perfectly regular, have undergone no loss of substance, and are not eroded and notched as in ostitis. Their thinness must be explained by the regular absorption of the surface, or by an arrest of development, an hypothesis which can only be considered in the case of young subjects in whom the bones are still growing. In these trabeculæ granulo-fatty degeneration of the bone corpuscles is noticed, with atrophy of their nuclei. To recognise this lesion the calcareous salts should be removed by macerating the trabeculæ for a few minutes in dilute hydrochloric acid, then washing with distilled water, and examining them after the addition of acetic acid; granules and droplets of fat are then seen to be present in the bone corpuscles, but the state of their nuclei cannot be clearly made out. To ascertain this, the trabeculæ should be placed for twenty-four hours in a ·2 per cent. solution of chromic acid; after which they are supple, showing that their calcareous salts have been dissolved out; they are then washed, placed on a slide, and stained with a solution of anilin in acetic acid; at the end of a minute they are again washed with distilled water and examined in water. With a lens magnifying 300 diameters it will be seen that in some corpuscles the nuclei have been preserved, but are irregular in form and surrounded with granules of fat; generally the corpuscles simply contain fat; some trabeculæ are found in which not a single corpuscle contains a nucleus. To observe these phenomena pieces of bone which have been dried in the open air must not be used, for as the bone dries the water evaporates, and the fat contained in the medullary spaces takes its place and forms granules and droplets of fat in the bone corpuscles. Fatty degeneration of the bone cells is only present in caries; it may be looked for in vain in dry arthritis, in rheumatism nodosum, in ankylosis, etc., in which diseases, nevertheless, the osseous extremities are friable and contain adipose medulla.

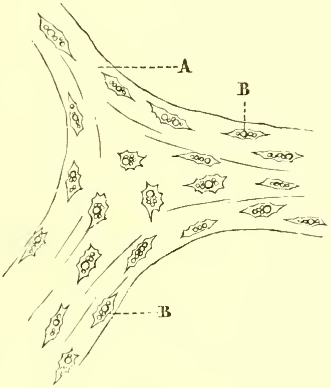

Fig. 192.—Osseous Trabecula of a Sequestrum of Caries in the Superior Extremity of the Tibia in a Child. It has been Decalcified by Weak Chromic Acid and Stained with Anilin Red.

a, ground substance of the bone transparent and without fatty granules; b, osseous corpuscles filled with fatty granules and containing no nuclei. Magnified 250 diameters.

Second period.—Fatty degeneration, characteristic of the first period of caries, is present also in the second. New lesions then occur, which are visible to the naked eye, and correspond exactly to the anatomical description of caries given by the older surgeons. These lesions are of an inflammatory nature, and seem to be caused by the presence of a large number of dead trabeculæ, irregularly scattered through the osseous tissue. The medulla becomes very vascular, the adipose cells disappear and are replaced by embryonic cells, and suppuration is established. The bone cells, which have escaped fatty degeneration, become active, the osseous substance surrounding them is dissolved, the necrosed trabeculæ become free, and granulations are formed from embryonic medulla. These granulations, which are very vascular, may attain a great size when located in an open space, such as a fistulous tract, or better still the cavity of an articulation. The dilated blood-vessels they contain often rupture, and cause both external and interstitial hæmorrhages. These large granulations form what are called *fungosities*. Similar but much smaller granulations are found welded together in the enlarged areolar spaces of the epiphyses, and osseous trabeculæ with cells infiltrated with fat are sometimes found imprisoned in their tissue.

Sequestra of caries.—In some cases, islets of osseous tissue become necrosed, and are surrounded with granulations which may penetrate even the substance of the trabeculæ composing the fragment. These carious sequestra are quite distinct from those caused by simple ostitis, for they are formed of trabeculæ which are undergoing fatty degeneration and which are thin but not notched; while the sequestra of ostitis always show, on the contrary, the characters of inflammatory rarefaction or condensation, and their corpuscles never contain fat granules. The sequestra of caries, in the form of delicate trabeculæ or larger fragments, may be dislodged by granulations and carried away by suppuration, if the fistulæ open externally; and in their place are left irregular cavities, lined with granulations which slowly undergo fibroid organisation; thus a kind of cyst is formed containing granular or caseous pus, and which may be often mistaken for old tubercle. In long-established and suppurating white swelling, islets, some centimetres in diameter, may sometimes be observed, formed of an ill-organised fibrous tissue, a firm and slightly fibrillated ground substance similar to that observed in old fistulæ leading to diseased bone. But at other times, there being no external outlet for the pus, carious sequestra may be found imprisoned, surrounded with granulations and infiltrated with caseous pus, the morbid mass having been isolated. Such foci closely resemble centres of puriform tubercular infiltration in process of elimination (to be described later); and it is probable that the two are often confounded; the distinction between them may be made by certain signs which will be indicated when treating of tubercle of the bones.

In caries, the embryonic medulla and voluminous granulations may undergo caseous degeneration for a more or less considerable extent. This change, probably due to vascular obstruction, was formerly considered to be of a tubercular nature.

Inflammation occurring in a bone affected with fatty degeneration is reparative when, by a process already indicated, it has succeeded in eliminating all the necrosed fragments ; it then becomes less intense, and the regeneration of the tissue commences. But long previous to this, there have been exuberant formations of bone at points near to the centre of the inflammatory focus, under the periosteum and particularly round the fistulous tracks. The new subperiosteal layers, which are then thick, are formed of delicate separate osseous lamellæ. The morbid process of caries being, however, very irregular, some parts of the bone have been long ago eliminated by the suppurative inflammation, while others only show some slight inflammatory lesion : in the former, eburnation is often met with, and in the latter rarefaction. This eburnation may lead to true necrosis by obliteration of the Haversian canals ; in which case, however, it is clear that irritation has been excessive.

In a bone affected with caries the course of the phenomena, such as we have described, is not identical in different parts of the bone ; only during the first period does an entire epiphysis have the same appearances throughout : in the second period, the osseous tissue varies in consistency and colour, which variations have been rightly considered characteristic of caries ; some portions are yellowish, semi-transparent, and slightly vascular, with delicate osseous trabeculæ (first period) ; others are vascular and purplish in colour ; some are whitish and opaque (caseous change, torpid or caseous caries of Billroth) ; here and there are spongy sequestra, partly detached, and surrounded with highly vascular fungosities (necrotic caries of Billroth) ; elsewhere there are islets of eburnated osseous substance ; finally there are upon the surface of the bone newly formed osseous layers, which are more or less extensive, thick, and stratified. After this description of caries, based on accurately observed facts, it is no longer possible to regard it as the same disease as simple ostitis, and, if inflammation plays an important part, it does not play the principal part, for the true though slightly apparent cause of caries is the primary fatty degeneration of the bone corpuscles.

V. Callus.

The name callus is given not only to the definite cicatrix which is formed between the two fragments of a fractured bone, but also to the new growth which precedes it. The anatomical phenomena in the evolution of callus are of a complicated character, and serve to connect inflammatory neoplasms and those constituting tumours. Fractures may be divided into three classes:—

1. *Compound, i.e.* those which communicate with the external air and are complicated with wounds; 2, *simple, i.e.* those not complicated with wounds; 3, *resulting from a friable and diseased condition of the bone,* as in cancer, rickets, etc. The two first only will be considered here.

I. **Compound fractures,** or those complicated with external wounds, are the most simple from the histological point of view, and are those in which bone is reproduced most rapidly. The phenomena are identical with those observed in ostitis. At all the irritated points on the surface of the solution of continuity, the medulla becomes embryonic, as in simple ostitis; under the periosteum the embryonic medulla throws out new osseous trabeculæ, which may be found there five or six days after the accident, whether the fracture be in man or experimentally produced in an animal; the Haversian canals, laid open by the fracture, enlarge by absorption of the osseous substance limiting them, and the medulla and blood-vessels which they contain concur in the formation of granulations; and the central medulla more slowly undergoes similar changes. Thus, over the whole surface of the solution of continuity, granulations spring up and, uniting together, constitute an embryonic or inflammatory tissue. In this embryonic tissue, which is also present at the base of the granulations, and which forms a mass varying in depth and extent, osseous trabeculæ are developed by the physiological process of ossification. Osseous needles spring from the old bone, which always seems to serve as the basis of the new growth, advance in every direction, and uniting with others near, and with those which spring from the opposite fragment, they limit spaces filled with embryonic tissue. These spaces are gradually lessened as fresh layers of osseous tissue are added, and thus consolidation is brought about by the solid adhesion of the two fragments of bone. In experiments made on small mammals, it is frequently found that suppurative inflammation is limited to the part in connection with the external wound, while cartilaginous masses are found in the deep part of the fracture which is not in contact with the external air. We shall show that cartilage is always produced in simple fractures uncomplicated with wounds. Suppuration continued for a variable time does not always prevent ossification. The process in its entirety does not differ essentially from condensing ostitis as seen in necrosis.

2. **Simple fractures** uncomplicated with wounds give rise, both in men and animals, to the production of a cartilaginous callus which subsequently undergoes ossification. Cruveilhier taught that 'the callus was formed by the ossification of all the soft parts which surround the fragments,' adding, however, that it was the connective tissue, whether in muscle or periosteum, which contributed to its formation. Opportunities are rarely found in practice of examining cases of simple fracture during the period of repair; but in old subjects affected with senile osteomalacia the occasion not unfrequently presents itself, and in these cases it is always found that consolidation of fracture is by means of a cartilaginous callus. The structure of callus in simple fracture can best be studied experimentally in animals.

The first phenomenon following fracture is hæmorrhage, which goes through all the phases of ecchymosis, and is generally so extensive as to gradually spread towards the skin. Soon phenomena due to irritation occur in the subperiosteal medulla and in the Haversian canals. This irritation, reaching the periosteum and the neighbouring connective tissues, causes proliferation of the cells, so that on the fifth or sixth day after the fracture all these tissues, rich in plasma and cells, concur in forming a single, firm, and consistent mass, which is, however, not yet cartilaginous. Under the periosteum and between the two fragments appears a thin, pulpy layer, in which, on microscopical examination, are seen cells of the varied forms of embryonic medulla, that is, small round cells similar to white blood corpuscles, round or irregularly shaped cells, 15 μ in diameter and containing one or more oval nuclei, and cells with peripheral buds (*vide* fig. 4). Among them red blood corpuscles and blood pigment are also found. This pulpy layer completely separates the mass of the peripheral embryonic callus from the bone; it is limited by the smooth internal pearly surface of the periosteum. When this pulpy layer is raised, the surface of the bone is completely denuded, and the Haversian canals are seen as red points or lines, just as in the commencement of ostitis. In a case of fracture of the clavicle with tearing of the periosteum, the pulpy layer of subperiosteal embryonic medulla was found at some spots to be more than a millimetre in thickness. In animals, when the periosteum has been torn, this layer is not so thick; it has even often escaped observation. If the irritation is not intense, the periosteum adheres to the bone as in the normal condition. At a later period, towards the eighth day, the cellular elements of the peripheral callus have multiplied to such an extent that the connective-tissue bundles and elastic fibres have almost entirely disappeared, while the blood-vessels, particularly on the border of the callus, have greatly developed. It is then, that is, from the eighth to the tenth day, that the cells of the peripheral callus are observed to become surrounded with cartilaginous substance, while the cells of the peripheral medulla still remain free. The peripheral callus is now cartilaginous, of the variety known as embryonic cartilage (p. 18), and is quite independent of the bone.

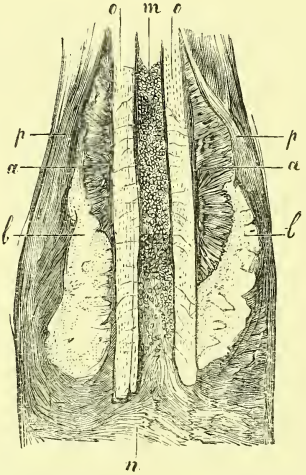

FIG. 193.—SUPERIOR FRAGMENT OF A FRACTURED TIBIA FROM AN ADULT WHITE RABBIT, AT THE END OF TWELVE DAYS.

The inferior fragment which was displaced is not included in the figure; in it the same layers were observed as in the part here represented. o, old bone; *m*, central medulla of the old bone; *a*, new bone in which embryonic medulla is abundant and causes the opacity observed in the drawing; the blood-vessels of this tissue are generally at right angles to the surface of the bone; *b*, cartilage; *m*, embryonic connective tissue intermediate between the two fragments, and penetrating into the medullary cavity; *p*, peripheral tissue blending with the periosteum. Magnified 20 diameters.

From the tenth to the fifteenth day the callus is infiltrated with calcareous salts, which appear in disseminated points near the bone; but calcareous infiltration is preceded by proliferation similar to that seen in the physiological ossification of a short bone.[1] Large cartilage capsules are observed filled with secondary capsules and opening into one another as the cartilaginous substance separating them becomes encrusted with calcareous salts; areolar spaces are thus formed, communicating with the periosteal medulla, and into which vascular branches from the blood-vessels of the old bone are pushed. Osseous trabeculæ are soon developed the bases of which are implanted on the old bone. In the majority of cases which we have examined, the first trace of ossification is not seen near the ends of the two fragments, but near the upper or lower borders of the callus. While bone begins to show at the margins of the callus, the formative cartilage increases between the two fragments, and undergoes calcareous infiltration, which infiltration invades parts of the cartilage where there has been no proliferation.

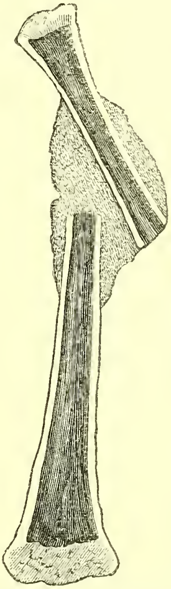

FIG. 194.—CALLUS AFTER SIMPLE FRACTURE OF THE TIBIA IN A RABBIT, ON THE TWENTY-SEVENTH DAY.

At this period—that is to say, from the fifteenth to the twentieth day—the callus is firm and resistant, but, though now solid throughout its entire mass, the whole of it does not undergo ossification. The peripheral parts, though infiltrated with calcareous salts, are not ossified; it being probable that they are absorbed without undergoing ossification. The part of the callus near the bone between the two fragments slowly ossifies and becomes finally converted into a solid mass, dividing the medullary canal into two portions; subsequently, and by a mechanism very imperfectly understood, this solid mass is perforated in the centre to re-establish the primary medullary canal. By the time that this final process has been effected, the peripheral callus has disappeared, so that in some cases it is difficult to believe that there has been a fracture. Hence Dupuytren had some reason in calling the peripheral callus the provisional callus. We have already said that all the soft parts surrounding a broken bone aid in the formation of callus; the muscles are no exception to this rule, as Cruveilhier pointed out; but it is not the muscular fasciculi themselves, but the inter-fascicular connective tissue, which is the active element. The muscular fasciculi undergo fatty degeneration, atrophy, and slowly disappear, and all those which are implicated in the formation of callus are lost to the organism.

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[1] These preparations are obtained from specimens of callus decalcified in a ·5 per 100 solution of chromic acid, or in a concentrated solution of picric acid.

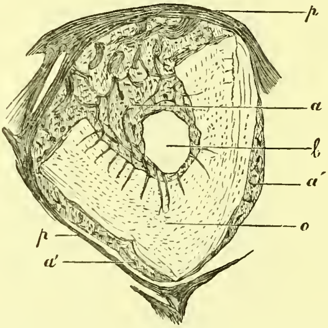

FIG. 195.—TRANSVERSE SECTION OF THE TIBIA OF AN ADULT WHITE RAT; CUT AFTER DECALCIFICATION IN A ·5 PER 100 SOLUTION OF CHROMIC ACID.

The bone was denuded in the living animal, and a wedge-shaped piece, *a*, about a centimetre in length, was removed with a scalpel. The gap has been filled up by new osseous tissue, and it is to be noticed that it has been deposited so as to give the bone its original shape twelve days after the operation; *p*, periosteum; *o*, old bone; *a*, new bone compensating for the loss of substance produced by the operation; *d*, new bone developed under the periosteum; *b*, medullary cavity diminished in size by the new osseous growth. Magnified 20 diameters.

Thus **two methods of formation of callus are observed**, according as the fracture is simple or compound; in compound fractures ossification takes place directly from embryonic and granulation tissue, while in simple fracture bone is formed from cartilage by the physiological method. In the present state of science it is impossible to explain what is the cause of this difference; the influence of the presence of bone in inflamed tissues cannot be adduced as the cause, as this occurs equally in both cases; neither can it be due to different degrees of irritation, for in condensing ostitis, whether acute or chronic, cartilage is not produced. If in a small mammal the bone is scraped so that the medullary canal is opened, the loss of substance is filled up by new osseous tissue, which is not preceded by cartilage, even if the wound unites by first intention, a result easily obtained in rats (*vide* fig. 195). These facts, which were discovered by one of us, have not met with attention; hence it is that Förster is unable to explain how, in man, he has never found cartilage in the callus, while in the rabbit fracture always cicatrises by means of cartilage. This arises from the fact that Förster, as well as most pathologists, have only had the opportunity of examining subjects who have died from serious compound fractures, while in experiments made on animals with the object of studying fractures, simple fractures only are produced.

VI. Tumours of the Bones.

Almost every kind of tumour previously described is met with in bones; but those most frequently seen are the principal varieties of sarcoma. In studying the seat of tumours of the bones an important distinction should be drawn between primary and secondary tumours. In the first case, it is generally the bones which are exposed to external injuries which are most frequently affected—the tibia and maxilla, for example. The bones most frequently attacked by secondary growths are, on the contrary, the vertebræ, sternum, and ribs—that is to say, those in which red medulla is present. Soft primary and rapidly extending tumours invade and destroy the osseous tissue as they progress. The bone is absorbed by a process similar to that of destructive ostitis. The morbid tissue of the tumour is not generally in contact with the osseous trabeculæ, being separated from them by a layer of embryonic tissue, from which the tumour develops. Sometimes the morbid process is continued to the extremity of the bone, but there, as in ostitis, it is arrested by a calcified layer of cartilage, which barrier is rarely passed, though in such cases subacute arthritis is generally present. Secondary tumours affect the bones much more frequently than is generally supposed; they can only be discovered by carefully made autopsies. The prognosis varies according to the nature of each tumour. We have nothing to add to what we have said regarding tumours in general, only that in tumours of the bone it must be noted that, the medullary system being continuous throughout the entire bone, tumours may find here a convenient nidus; and if in an operation the apparent tumour is alone removed, the adjacent part of the bone being left intact, a recurrence of the growth almost always follows.

Species and varieties of tumours of bone. — **Encephaloid sarcoma** is common in bone (p. 135), where it may attain a large size and spread rapidly; it not unfrequently assumes the erectile form, and in bone may give rise to symptoms which have been clinically ascribed to aneurism of the bone. The vascular dilatations, caused by the return of the walls of the capillaries to the embryonic state, may be so large, and the communications established between them sometimes so extensive, that one large sac may be formed. Inside this sac delicate, soft, and floating septa may often be found, the structure of which is the same as that of the tumour. On a superficial, naked-eye examination, such a growth might easily be mistaken for aneurism of the bone. Hæmorrhagic foci and cysts due to mucoid degeneration may also be observed (*vide* p. 147) in encephaloid sarcoma of bone.

Fasciculated sarcoma is much more common in bone than the preceding. The arrangement of the tissue in fasciculi is more or less complete, to which is due the firmness of these tumours, varying from that of encephaloid to that of fibroma, so that it is often difficult to distinguish between encephaloid and fasciculated sarcoma, particularly in those rather common cases in which the two morbid varieties are united in the same tumour. Soft fasciculated sarcoma is often observed in the substance of the bone, while hard fasciculated sarcoma is more frequently subperiosteal. In fasciculated sarcoma of the bones, large giant cells—the largest found anywhere—are frequently observed; but the presence simply of these cells is not sufficient to characterise any particular species of tumour, and to indicate, as Nélaton thought, that the growth was consequently benign. These cells are, in fact, met with in every kind of sarcoma both of the bones and of other organs. Both encephaloid and fasciculated sarcoma very often become incrusted with calcareous salts; this lesion has no influence on the prognosis. The change generally occurs in the form of needles or friable trabeculæ, in which the cells of the morbid growth are found inclosed in small lacunæ without processes. Bones, affected with sarcoma, are very easily fractured at the diseased spots, and from the sarcomatous tissue islets of cartilage are formed which do not, however, succeed in producing a solid callus. This fact seems to indicate that fracture acts on morbid tissue in the same way that simple fracture acts on the normal tissues surrounding it.

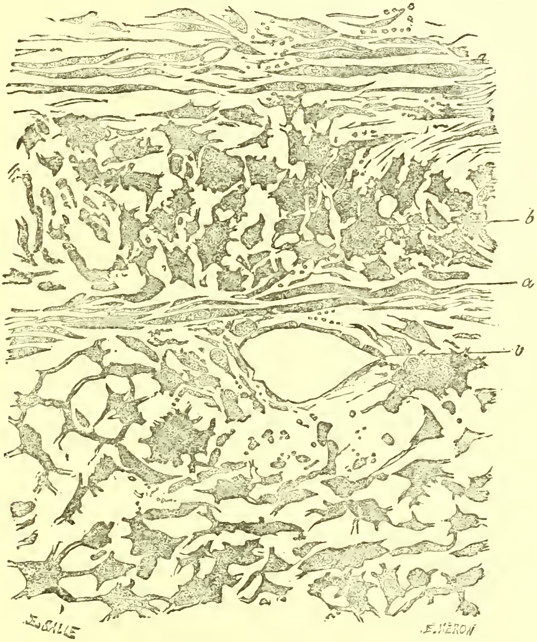

Fig. 196.—Section of a Fasciculated Sarcoma.

a, sarcoma cells arranged in fasciculi and seen sideways; *b*, cells of the fasciculi placed at right angles to the former; *v*, blood-vessel showing a row of flat cells in its wall. Magnified 20 diameters.

In **myeloid sarcoma** the tissue is soft, like that of the fœtal medulla of bones, and has moreover the same histological characters. It is composed chiefly of round transparent cells, larger than normal; mother-cells are sometimes numerous; the walls of the blood-vessels are normal, and do not become embryonic. We have seen a tumour of this kind almost entirely destroy the tibia.

Ossifying sarcoma is a very common species; it is that which forms almost all the epules, subungueal tumours, and many of those tumours known in France under the name of *tumours of myeloplates* (tumeurs à myéloplaxes). All the latter are, however, not ossifying sarcomata, so that the terms are not synonymous, for fasciculated sarcomata may contain a great number of giant cells, but they must not be confounded with ossifying sarcomata, which are relatively benign, while fasciculated sarcoma is extremely malignant.

Lipomatous and **melanotic sarcomata** are also met with in bone, the latter are secondary growths (*vide* fig. 199).

Myxoma is found in bone in the form of a globular, clearly defined tumour. It is generally developed under the periosteum, and causes an absorption of the bone which supports it; we have never seen it infiltrate the osseous tissue in a diffuse manner. With myxoma must not be confounded a nutritive lesion of the marrow of the bone, which is seen when cachetic conditions have existed for a long time, and which is characterised by a gelatinous appearance, due to the more or less complete absorption of the fat of the adipose cells, and its substitution by serum or plasma.

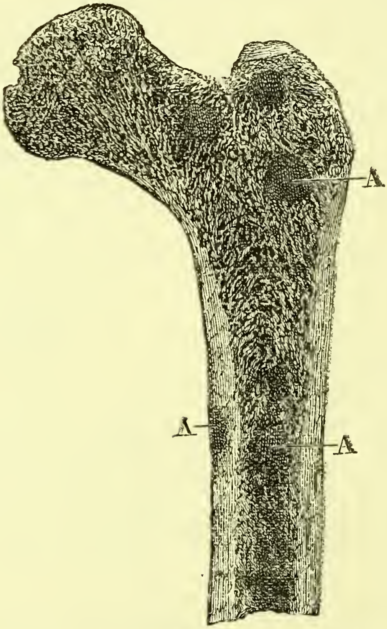

FIG. 197.—SECONDARY MELANOTIC TUMOURS OF THE FEMUR, AND MELANOTIC INFILTRATION OF THE BONE MEDULLA.
After Benjamin Anger and Worthington.

Lipoma.—We have seen but one case of lipoma of bone; the tumour was very large, and had developed in the body of the tibia; the lobules of adipose tissue, instead of being bounded by fibrous septa, were separated by osseous trabeculæ.

Carcinoma.—In bone is found every species and variety of carcinoma; we have seen well-authenticated cases of primary carcinoma in bone, but secondary growths are much more frequent; thus, scirrhous carcinoma of the breast of long duration is almost always accompanied by secondary nodules in the vertebral column, which rarely develop into large tumours, the morbid tissue being more often substituted for the osseous tissue, so that a bone, a vertebra, for example, may be almost entirely composed of carcinomatous tissue, without its showing any marked change in form. There may even be considerable atrophy of bone without ulceration or erosion. If one or more vertebræ are affected with carcinoma and they break down, being in a friable state, such a loss of substance may be occasioned that curvature of the vertebral column may result, as in Pott's disease. When developed in the body or extremities of the long bones, spontaneous fractures may occur, followed by extravasation of blood; but we have never seen the least attempt at repair by ossification, the irritation only resulting in the transformation of the neighbouring tissues into carcinomatous tissue. The development of carcinoma in bone has been described at page 176.

Tubercles are generally observed in the cancellous tissue of long or short bones, but their seat of predilection is the bodies of the vertebræ, the sternum, and the ribs. It is in these places that general miliary tuberculosis is most frequently met with, and where the interesting evolution of tubercle can be most easily followed. In the adult, the medulla of the sternum, ribs, and bodies of the vertebræ is red, inclining to violet, and slightly translucent. It is composed of the usual medulla cells, a few scattered fat cells, and blood-vessels, around which there is a delicate layer of ordinary connective tissue. An isolated tubercle in such a tissue is so distinctly characteristic that it is impossible to mistake it; it forms a circular spot, one to two mm. in diameter, quite bloodless, semi-transparent, and often with a slightly irregular border; in the centre it is frequently opaque, while at its periphery the medulla is of a deep red colour. The tubercular nodule cannot be felt with the finger, owing to the presence of osseous trabeculæ. The semi-transparent, grey granulation of osseous tissue can thus be distinctly recognised with the naked eye; but to make a thorough examination, the method of preparing the bone is not a matter of indifference. After dividing the bone with a saw, the surfaces should be scraped with a strong scalpel. The bone may be equally well divided by means of a blunt wedge and a hammer, for even the finest saw produces a great deal of debris on the surface of the bone, and completely changes its appearance. In bone thus prepared discrete tubercular granulations can be distinctly seen, for they show plainly in the midst of a highly coloured tissue; but if the granulations are grouped together in the same medullary space, their recognition becomes impossible without recourse to the microscope. Confluent granulations form irregular masses varying in diameter from three to four mm. to many centimetres. At the beginning of the process it can be easily seen that large masses are formed by the union of a certain number of smaller masses; in form these are generally very irregular, and there is nothing in their appearance to lead any one, who had not already examined similar growths under the microscope, to guess what was their true nature, and even such a one might be deceived. They are bloodless, granular, grey, and semi-transparent, at some places they form very small opaque spots, which in the older growths, by extending and blending together, give a decidedly caseous appearance to the morbid mass. The osseous trabeculæ which are contained in the midst of this caseous mass are most frequently intact. At the border of the entirely caseous parts there are two zones, the most internal of which is narrow, anæmic, and semi-transparent with opaque spots; the external is a deep red, not transparent, and melts gradually into the violet medulla. In some cases when the formation of tubercle has been rapid and has occurred simultaneously at a great number of spots, the medulla of the entire bone (sternum, bodies of the vertebræ) is of a very dark red. In such cases also the osseous framework is seen to have undergone rarefaction.

There are therefore two varieties of tubercle in bone: *discrete tubercular granulations*, and *confluent tubercular granulations.*

Discrete tubercular granulations in bone.—If a tubercle in bone be removed with a cataract needle, it looks like a small, round, or slightly angular mass. Placed on a slide in a drop of water and examined without being covered with a cover-glass, with a power magnifying 150 diameters, the mass appears to be composed solely of medulla cells movable on one another; but this appearance is an illusion caused by the mass being completely enveloped by medulla cells; in fact, if the granulation be washed with a camel's-hair brush, it is found that it cannot be disintegrated, and, on examining it again after covering it with a cover-glass, very small cellular elements ($5\ \mu$ to $7\ \mu$) are perceived, immersed in a granular, or slightly fibrillar substance; if the centre of the granulation is already caseous, this part appears opaque. But this process is very imperfect, and, to study tubercle well, delicate sections should be cut after maceration in ·5 per 100 solution of chromic acid. To decalcify the specimen so as to cut sections of the osseous tissue with a razor, time, varying according to the size and density of the fragment, is required. To complete the hardening process, and to retain the cellular elements *in situ*, it is well to afterwards employ gum and alcohol. A granulation seen in a section has, under the microscope, the following characters: at its periphery the medulla is observed to contain no fat cells, the blood-vessels are dilated, and no longer have connective tissue around them. This zone of irritation often extends to many areolæ of the spongy tissue, in which the osseous trabeculæ are found notched as in ostitis. These phenomena of irritation are not only observed round the granulation, but at points far removed, so that it is logical to suppose that formative irritation precedes the appearance of granulations; in one word, that in bone, ostitis precedes tubercle. The tissue of the granulation is composed of small, refractive cellular elements, which diminish progressively in size

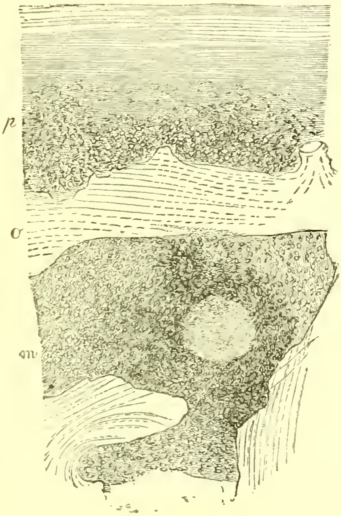

Fig. 198.—Discrete Tubercle of the Sternum, from a Case of Acute Tuberculosis.

p, periosteum of the anterior surface of the sternum with thick embryonic subperiosteal layers as in ostitis; *o*, first osseous layer in which the lamellæ are irregularly notched by the inflammatory process; *m*, embryonic medulla in the midst of which a tubercle is seen surrounded by a dark zone produced by vascular dilatations and hæmorrhages. Magnified 20 diameters.

from the periphery towards the centre; they are contained in a firm granular substance.

Confluent tubercular granulations in bone.—It is probable that some of the changes which Nélaton described under the name of tubercular infiltration were lesions caused by confluent tubercular granulations; but his description applies equally well to caries with caseous degeneration of the pus, to eburnated sequestra, and to certain syphilitic gummata. In fact, without the microscope, it is often impossible to know if a lesion be tubercular, for though the granulation is the unique characteristic product of tuberculosis, yet confluent tubercular granulations cannot be diagnosed with the naked eye. When a great number of granulations are formed contemporaneously in the same medullary space (*b*, fig. 181), they do not attain so large a size as discrete granulations, they rapidly undergo caseous degeneration, and induce a similar degeneration of the medulla contained between them. The development and structure of tubercle are always identical, whether the granulation be discrete or confluent. It is now proved that a tubercular granulation developed in bone causes the obliteration of the blood-vessels which traverse it; hence it is obvious, that if many granulations are scattered over the same medullary space, the circulation in all the vascular branches of this space may be

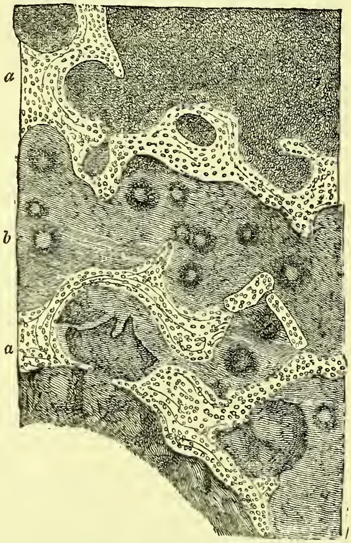

FIG. 199.—CONFLUENT TUBERCLE IN BONE.
a, osseous trabeculæ; *e*, embryonic medullary tissue; *b*, tubercles.
Magnified 20 diameters.

arrested; if, moreover, some areolæ of spongy tissue, free from granulations, were surrounded by areolæ filled with tubercle, they would also have their blood-supply cut off. All parts of the bone in which the circulation has been arrested undergo caseous degeneration, for the same reason that infarcts become caseous. The areolæ, which have become caseous from vascular obliteration, frequently have a different appearance to those which have undergone the same change from breaking down of tubercular granulations. In the former, the adipose cells are preserved, or their place is marked by groups of stearic acid crystals; in the latter, the adipose cells, having disappeared in the ostitis which preceded tubercle, have left no traces.

Caseous degeneration of the medulla.—The medulla in undergoing caseous degeneration first becomes semi-transparent, and the medulla cells seem pressed and blended together; but this condition does not last long, and is observed only in a very limited area; it is soon followed by caseous degeneration, when what was previously medulla and tubercle are no longer distinguishable. The osseous trabeculæ contained in a caseous mass do not generally undergo either condensation or rarefaction. Except in tuberculosis it is rare to find such extensive lesions of osseous tissue without rarefaction; we have, indeed, seen cases in which bones, or fragments of bone, have remained in the midst of a mass of caseous pus, without being either wholly or partially dissolved; while osseous trabeculæ, even when necrosed, which are in contact with an active medullary growth, are generally absorbed. When, in consequence of the tubercular process, the areolæ of the spongy tissue become rapidly filled with a caseous mass resulting from the degeneration of the granulations or of the intermediate medulla, it is comprehensible that the adjacent osseous trabeculæ may persist indefinitely. The bone corpuscles are not implicated in the caseous degeneration of the elements of the medulla; their nuclei become irregular, but there are no fatty granules around them. This fact, ascertained by means of staining with anilin red, allows of the distinction being made between caseous degeneration following confluent tubercle and that which accompanies caries. While in the latter the bone corpuscles undergo granular fatty degeneration, the bone tissue affected by tuberculosis becomes necrosed by having its blood-supply cut off, and elimination occurs when the tubercular eruption has reached a certain point. Elimination probably occurs in the same way as in simple necrosis, that is, as the result of rarefying ostitis which, set up on the margin of the tubercular centre, determines the absorption of the osseous trabeculæ and the formation of granulation tissue. In this manner a cavity is formed which lodges for a longer or shorter time a sequestrum bathed in pus. If in bone a cavity is found, lined either with granulations or a smooth membrane, and which is filled with pus or caseous matter, it cannot, in the present state of science, be concluded that it is of tubercular origin, unless tubercular granulations are found in the peripheral tissue. A sequestrum of cancellous tissue immersed in pus or infiltrated with caseous matter cannot be attributed to confluent tubercle, unless confluent or discrete granulations are found in the surrounding bone tissue. In fact, simple ostitis, caries, and gummata may in osseous tissue produce changes which, in their naked-eye appearances, resemble confluent tubercle in the period either of evolution or of elimination.

Gummata of the bones have been studied by Dufour, Gosselin, Virchow, and ourselves. Like tubercle, they are frequently located in the bones which contain red medulla; in the bones of the skull, however, in which tuberculosis is unknown, gummata are frequent. Anatomical descriptions of gummata of the bones are rare, for, though they are clinically common, patients rarely succumb to syphilis. Gummata of the bones are seen under two forms: well defined, with the appearance and consistence of sarcoma, or infiltrating the osseous tissue, and justifying the name of gummatous osteomyelitis which has been given them.

Circumscribed gummata have been studied by Virchow in the bones of the skull. We have ourselves seen many cases. They first develop under the epicranial periosteum or above the dura-mater, and sometimes simultaneously at both these points; they advance in a conical form into the osseous tissue, of which they determine progressive rarefaction (the structure of gummata has been described on p. 191). They then undergo caseous lardaceous change, and, if the description given by Virchow be accepted, they are slowly absorbed, probably as the result of treatment. In their place is formed a stellate cicatrix of osseous tissue mixed with fibrous tissue. Notwithstanding that Virchow allows that these cicatrices are those of old gummata, he calls them by the name of *dry syphilitic caries*. It is evident from the description we have given of caries that there is nothing in common between this lesion and that caused by syphilis. Those singular losses of substance, which are truly characteristic of syphilis, are bounded by sclerosed osseous tissue, and are often surrounded by flattened osteophytes.

Diffuse gummata are particularly frequent in bone which is subcutaneous, and in the palatine arches. They develop simultaneously under the periosteum and in that portion of the bone covered by it, in the form of a soft, slightly gelatinous tissue, which is at first rose-coloured, but subsequently becomes opaque and firmer. On section of the bone at this stage a whitish surface is seen, caseous in appearance and resembling confluent tubercle; but a phenomenon which will serve to differentiate the bone is already present, and is to be found in a white pulpy layer which is seen under the periosteum over the area corresponding to the bone lesion. In delicate sections, made after maceration of the bone in a ·5 per cent. solution of chromic acid, the osseous trabeculæ are seen to be notched as in rarefying ostitis, and the enlarged medullary spaces contain gummatous nodules (*vide* p. 333), in which the blood-vessels are permeable, a fact which differentiates them from tubercle. At the margin of the gummata there are all the appearances of simple ostitis.

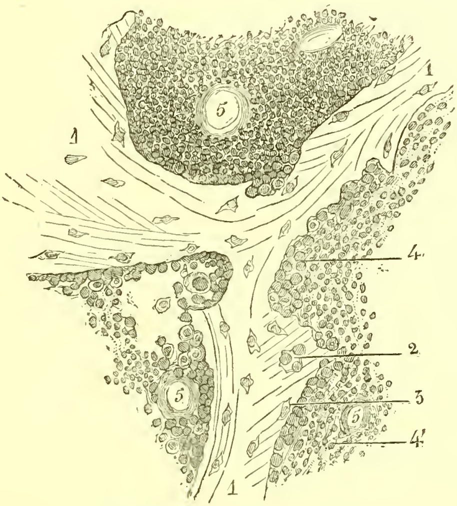

Fig. 200.—Syphilitic Ostitis.

1, osseous trabeculæ with eroded and dentate borders, in which, at 3, uni-nucleated bone corpuscles are seen, and multi-nucleated at 2; 4, medullary tissue; 5, blood-vessels of which the lumen is patent. At the upper part of the figure the cells are atrophied and are undergoing caseous change.

To the question what becomes of diffuse gummata of the bone, an answer cannot be given based on an accurate knowledge of consecutive histological facts; we only know from clinical observations that gummata, for example those of the sternum and tibia, may completely disappear under the influence of anti-syphilitic treatment, and leave in their place hyperostoses similar to those which accompany circumscribed gummata of the frontal bone. Cases of syphilitic necrosis have, moreover, been observed in which the sequestra, instead of being eburnated, are, on the contrary, found to be riddled with numerous cavities filled with a caseous detritus at the moment of examination, and which probably formerly contained gummatous tissue. Virchow even thinks that every case of syphilitic necrosis has a similar origin, but we consider that necrosis of the bone very often results from condensing ostitis or sclerosis, continued till the vascular canals are obliterated.

Chondromata of bone.—Osseous tissue is more often affected by chondromata than any other. They are called **perichondromata** when located under the periosteum, and **enchondromata** when developed in the substance of the bone itself. They may be diffuse or lobulated: the latter is the more common variety. All the varieties described on page 215 may be met with in bone, namely, hyaline, ossifying, mucous chondromata, lobulated or fibro-cartilaginous chondromata, or the variety formed of branching cells. They develop in the way we have already described (*vide* p. 219), and we have nothing to add regarding their prognosis (*vide* p. 222). Primary osteoid tumours are always developed from osseous tissue. (For description of them see p. 222.)

Osteomata of osseous tissue are called exostoses, hyperostoses, or osteophytes, according to the form affected on the surface of the bone (*vide* p. 225). The name of enostoses has been given to those osseous growths which are developed within the medullary canal. Osseous tumours found in other organs will be described when treating of the organs in which they are met with.

Lymphadenoma of bone.—In leucocythæmia, lymphatic tumours or lymphadenomata of the bones may be met with. In a case which we published in 1867 the tumour was of considerable size: it was composed of a whitish tissue, which on scraping yielded a milky juice, which contained cells resembling white blood corpuscles. At some points the tumour had undergone caseous degeneration. In sections cut after hardening in alcohol and chromic acid the retiform stroma of adipose tissue was found everywhere. With the unaided eye this tumour might have been mistaken for carcinoma.

Since this first case, several similar ones have been published, particularly by M. Kelsch.

Epithelioma of bone.—It is doubtful if there has ever been a case of primary epithelioma of bone, but its extension from neighbouring tissue is common. Thus epithelioma of the lips may be propagated to the maxilla; that of the palate to the palatine arch, that of the limbs may become deeper and attack the underlying bones. The morbid growth develops by means of epithelial buds, which are pushed forward and grow in the midst of an embryonic tissue, which is itself formed from osseous tissue as in ostitis (*vide* pp. 265 and 266, and figs. 154 and 155). Tubular pavement epithelioma is met with in bone; it is rather frequent in the superior maxilla, where it is consecutive to tumours of the soft palate and the Antrum Highmori; lobulated epithelioma is also observed here, where it is consecutive to cancroid of the lips. A single case of cylindrical-celled epithelioma has been reported by Gawriloff, which is not surprising considering that this form of epithelioma causes secondary growths like carcinoma.

Cysts, showing all their usual characters, are sometimes met with in bones.

VII. Osteomalacia.

True osteomalacia is a disease which is most frequently seen in women after one or many confinements. It has become extremely rare in France, while it is observed rather frequently in Bavaria. It is characterised by a nutritive lesion of the bones, which terminates in absorption of the calcareous salts and solution of the osseous trabeculæ; at the same time, important changes take place in the medulla. In the first period the volume of the bones is preserved, and there is no rarefaction; they can, however, be cut through with a sharp knife. Under the microscope it is then seen that the centre of the osseous trabeculæ contain calcareous salts, while the margins are quite deprived of them. According to Rindfleisch these parts stain with carmine. Now it is known that a non-decalcifying bone does not stain with carmine. The bone corpuscles are similar to those obtained in preparations of bone decalcified by chromic or hydrochloric acid. The blood-vessels of the medulla are full of blood. The fat cells are less abundant than usual, and in their place are found cells which may be round or irregular, fusiform or flat. Hæmorrhagics soon occur in the medulla, and appear as ecchymotic spots or foci; they may also take place under the periosteum, which adheres but feebly to the subjacent osseous tissue. In a second period the bones undergo considerable changes of form: they bend over, fall together, and become fractured, and it is then that those extraordinary malformations are seen of which so remarkable a specimen is preserved in Dupuytren's Museum (Paris). The osseous trabeculæ are then not only decalcified throughout their whole thickness, but are also partly absorbed. The enlarged medullary spaces are filled with a fœtal medulla having the appearance of splenic pulp. In consequence of extravasations of blood, the hæmoglobin of the blood; in the form of yellow, red, or brown pigment, is frequently found in the medullary cells. The fractures produced in osteomalacic bones do not generally unite well, though some cases of bony union have been reported, but in these cases the disease was progressing towards cure. A satisfactory explanation has never yet been given of the decalcification and absorption of the osseous tissue. An attempted explanation has been given by the formation of an acid which dissolves out the calcareous salts; what this acid is, is not known. Weber has found free acid in the urine of osteomalacic patients; Rindfleisch thinks that the solution of the calcareous salts might be attributed to an excess of carbonic acid gas; he considers that the venous congestion of the medulla, observed in the first period,

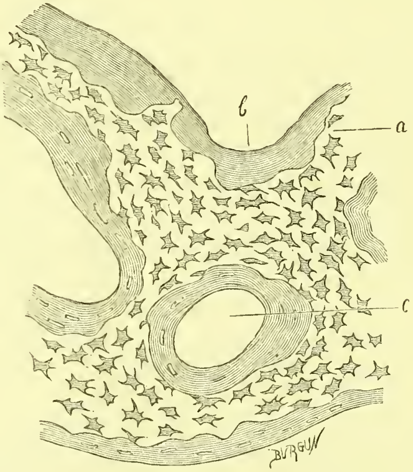

FIG. 201.—SECTION OF THE CANCELLOUS SUBSTANCE OF A RIB AFFECTED WITH OSTEOMALACIA.

a, normal osseous tissue; *b*, part deprived of calcareous salts; c, Haversian canal. Magnified 300 diameters. (After Rindfleisch.)

is caused by stasis, and hence that the blood is charged with carbonic acid, which being brought into relation with the osseous trabeculæ dissolves out the calcareous salts. This is, however, only an ingenious hypothesis.

Senile osteoporosis.—Under the name of senile osteomalacia has been described rarefaction of the osseous tissue caused by enlargement of the medullary spaces. In this disease the friability of the bone is simply related to its rarefaction ; there is not here, as in true osteomalacia, softening due to decalcification. The rarefaction of the bone is accompanied with important changes in the medulla, similar to those observed in true osteomalacia. They consist in the disappearance of the adipose cells, and the formation of cells similar to those of fœtal medulla. Sometimes young connective tissue of new formation is produced in the medullary spaces. The bones most frequently affected with this disease are the ribs and the vertebræ. The vertebral column bends, the ribs fracture from the slightest exertion, and curiously enough perfect consolidation is effected by the ossification of a cartilaginous callus.

Adipose osteoporosis.—We call by this name a form of rarefaction of the bone; it is seen particularly in the epiphysial extremities of the long bones or in short bones, and is characterised by an abundant formation of fat cells in the medullary spaces and Haversian canals. The osseous trabeculæ of the spongy tissue become very thin and finally disappear ; the bone is then reduced to a parchment-like shell pierced with numerous vascular holes. Adipose osteoporosis is met with in cases where joints have been long immobilised, and in chronic articular affections.

VIII. Rachitis.

Rachitis is a disease of the bones occurring during the period of active growth. It is histologically characterised by disturbances of nutrition, and the formation of tissues which tend towards ossification. These tissues are the epiphysial cartilages, the periosteum, and the medulla. Rachitis is a very common disease, especially in large towns and among the children of the poorer classes. In the first period of the disease, rachitis exhibits no deformity, and, to ascertain its frequency, the bones of all cadavers of children should be examined. Three periods may be distinguished in rachitis : in the first the affected bones are not deformed ; in the second there are considerable deformities ; and the third period is characterised by consolidation of the diseased bones. If the histological lesions be alone considered, there is no well-marked difference between the first and second periods: the same process continues, extends, and causes modifications appreciable in the living subject. We will now proceed to study the evolutions of these lesions in the cartilage of ossification in the medulla and in the periosteum, comparing them constantly with normal ossification.

Normal ossification of cartilage occurs with great regularity (*vide* p. 22). The cells of the fœtal cartilage swell, while the capsules surrounding them become spherical; the cells then divide and become surrounded with secondary capsules, so that each primary capsule contains four to ten secondary capsules. The enlarged primary capsules elongate by reciprocal pressure, so

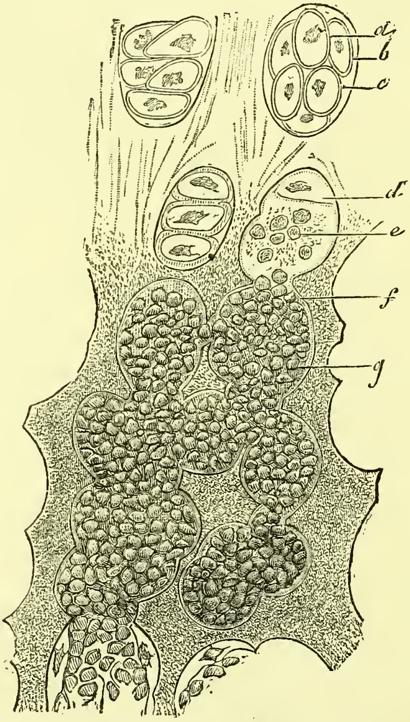

FIG. 202.—OSSIFICATION FROM CARTILAGE.

a, primary capsule filled with secondary capsules; *d*, cartilage cell, the capsule of which is about to disappear; *e*, proliferation of the cells which eventually form the embryonic medulla; *g*, the spaces filled with this new medullary tissue are bounded by the calcified ground substance. At the lower part of the figure, stellate bone corpuscles are already apparent. Magnified 250 diameters.

as to converge towards the point of ossification. The layer in which these phenomena occur is bounded by two parallel lines from 1 mm. to $1\frac{1}{2}$ mm. apart; this layer is visible to the naked eye by its semi-transparent and bluish look, placed as it is between the ossiform and cartilaginous tissues. It has been called *chondroid* by Broca, a name which however gives the impression that it is formed of a tissue having only the appearance of cartilage, though it is in reality formed of cartilage in a state of proliferation.

At **the commencement of rachitis** changes are observed in this layer which are continued during the whole course of the disease. With the naked eye the layer is seen to have increased in thickness; it may even attain a diameter of many centimetres. Instead of being regular, its margins, both on the cartilage and the bone side, are very irregular and sinuous. Sometimes it sends out long processes into the bone which frequently form separated fragments by thinning of their bases. The layer is moreover furrowed by medullary canals of cartilage containing dilated blood-vessels. On microscopically examining preparations of this layer, its resemblance to cartilage undergoing physiological proliferation is very striking. The primary capsules are however much longer, and contain a greater number of secondary capsules, which are also more voluminous. Beneath this layer, and continuous with it, there is a red, vascular, spongy tissue, of a consistence similar to that of bone partially softened by an acid. To perfectly under-

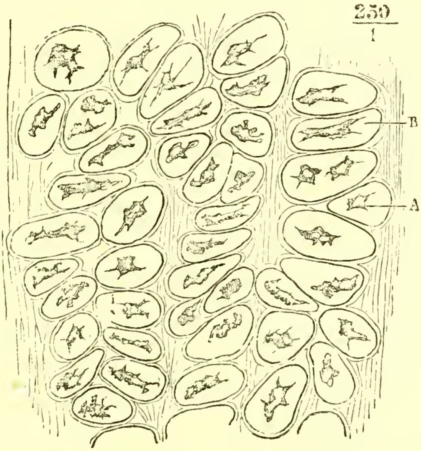

FIG. 203.—ZONE OF PROLIFERATING CARTILAGE IN RACHITIS.

A, cells pressed together and stained brown-violet with an aqueous solution of iodine, which stain is due to the glycogenic matter they contain. B, secondary capsule. Section made in the fresh state and examined in water.

stand the significance of this layer, the tissue which normally exists at this spot must be considered. Beneath cartilage which is proliferating there is normally a thin layer formed of areolar tissue, the trabeculæ of which are composed of a cartilaginous matrix infiltrated with calcareous salts; the alveoli contain embryonic medulla and blood-vessels. Beneath this true osseous tissue is formed. We have given the name of *ossiform* to this layer which is interposed between the cartilage and bone. In rachitis there is not, as Broca thought, a simple increase of this layer, but the formation at the same level of a peculiar tissue, to which Guérin has given the name of *spongeoid*, because of its spongy appearance.

Spongeoid tissue.—This tissue, which often extends from the margin of the cartilage to the diaphysis, sometimes even invading it, is red, composed of very irregular alveoli, and seems to contain much blood. The tissue is of the same consistence as a fine sponge, or as the osseous tissue of an epiphysis partially softened by an acid. The boundary line between this spongeoid tissue and cartilage is, though sinuous, very distinct. Sometimes islets of hyaline cartilage are found in the midst of it, so that it is often quite impossible to indicate in a precise manner where the old bone ends. At the level of the periosteum the spongeoid layer becomes blended, particularly on the margin of the diaphysis, with a tissue formed of nested ossiform lamellæ, separated from one another by a soft tissue described further on. In microscopic examination of fresh sections, the trabeculæ of the spongeoid tissue are seen to contain angular corpuscles irregularly scattered through a granular and non-laminated substance. These corpuscles, larger than bone

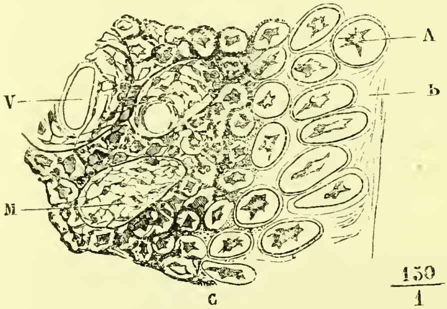

FIG. 204.—RACHITIS. FORMATION OF SPONGEOID TISSUE FROM PROLIFERATING CARTILAGE.

A, cell shrunk by action of the reagent; B, segmented ground substance; C, ground substance infiltrated with calcareous granules; M, medullary cavity filled with young connective tissue. V, vessel.

corpuscles, have no anastomotic canaliculi. To understand the significance of the tissue composing these trabeculæ, its development from hyaline cartilage should be followed. Calcareous infiltration of the segmented ground substance which separates the large capsules is observed; but the infiltration also extends to the secondary capsules, which never occurs in physiological ossification; hence we find the cartilaginous tissue invaded throughout its entire mass by calcareous granules, which remain distinct, that is to say, separated from one another by a cartilaginous substance which retains its flexibility. The secondary capsules are not dissolved, which is essentially different from what occurs in physiological ossification. At the same time that this calcareous incrustation is taking place, the vascular canals of the cartilage, springing from the medullary cavities of the old bone, enlarge by solution of the calcified tissue surrounding them, and opening into one another form a cavernous system, the contents of which will be described further on.

Spongeoid tissue is thus seen to be formed of trabeculæ representing portions of cartilaginous tissue infiltrated with calcareous salts. When young the cartilage and corpuscles can still be recognised, though the margins of the capsules are often difficult to distinguish owing to calcareous incrustation. In older trabeculæ the capsules are quite hidden, but to render them apparent all that is necessary is to dissolve out the calcareous salts by dilute hydrochloric acid or a ·5 per 100 solution of chromic acid. But even these reagents may not be able to reveal the presence of the cartilage capsules; angular corpuscles embedded in a ground substance, which appears homogeneous after the calcareous salts have been dissolved out, being all that is recognisable. Lamellæ, similar to those observed in normal osseous tissue treated by acids, are never seen in these trabeculæ. The cavities bordering the trabeculæ of spongeoid tissue continue to enlarge, which is the reverse of what takes place in normal ossification when the medullary spaces become narrowed by new osseous deposits.

Changes in the medulla.—The medulla contained in the spaces of the spongeoid tissue is at first fluid, red, and composed of round or angular cells, some of which are pigmented; there are besides numerous red blood corpuscles; but in the older medullary spaces the contents are more consistent; the cells become stellate in form and are separated by a slightly fibrillated ground substance. This effort at fibrous organisation of the medulla takes place, not only in the medullary cavities formed during the evolution of rachitis, but also in the old medulla contained in the cancellous tissue and Haversian canals, as well as in the central and the sub-periosteal medulla. In the central canal the peripheral layers of the medulla are those which are most modified. Often in pronounced cases of rachitis, while the centre of the marrow is red, fluid, and in a fœtal condition, the periphery is organised into a kind of young connective tissue which has the appearance of a medullary membrane. It is possible that it was this appearance which led the older pathologists to admit the existence of a medullary membrane, not visible in any other case.

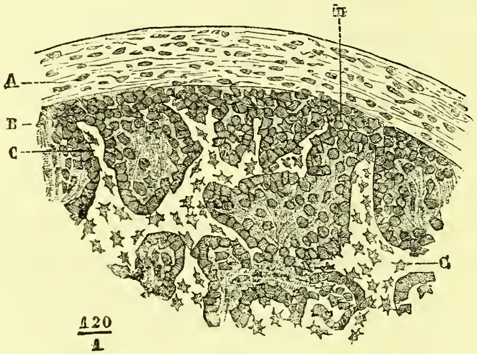

FIG. 205.—SUB-PERIOSTEAL OSSIFICATION.

A, transverse section of the periosteum showing connective-tissue cells; B, medullary tissue; C, osseous trabeculæ containing stellate osseous corpuscles. All along the osseous trabeculæ there is a close layer of medullary cells flattened by reciprocal pressure. Many of these cells may be seen undergoing transformation into bone corpuscles. Magnified 120 diameters.

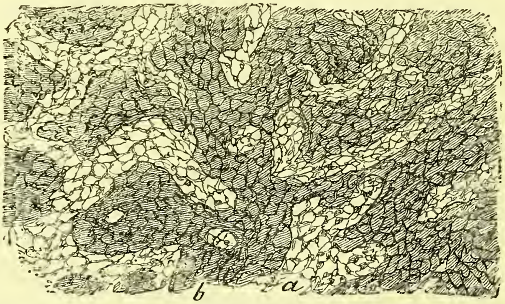

FIG. 206.—OSTEOID TISSUE FORMED UNDER THE PERIOSTEUM IN RACHITIS.

a, osteoid trabeculæ; *b*, connective tissue contained in the medullary spaces.

The sub-periosteal layer of medulla, to which we have often referred, is transformed at the commencement of the disease into a soft connective tissue, which at a more advanced period becomes more solid. It is adherent to the internal surface of the periosteum and to the surface of the bone, so that the two cannot be separated, which is generally easily done in young subjects. This layer of connective tissue, which is truly sub-periosteal, may attain considerable thickness. It undergoes an important change, which consists in the appearance of refractive trabeculæ, which curve over and unite with one another. These trabeculæ are the analogues of Sharpey's fibres, which are observed in the ossification of the secondary bones of the skull, and of the arciform fibres of a nodule of ossification. They differ from them, however, by containing cells. The tissue in which these trabeculæ are developed is considered by Virchow as representing the first phase in the process of ossification, and hence is called *osteoid tissue* by him. We have already seen (*vide* p. 222) that tumours may be composed of the osteoid tissue of Virchow. Sections of the tissue cut perpendicularly to the axis of the bone, stained with carmine and treated by acetic acid, show throughout the preparation, in the refractive trabeculæ as well as in those parts which have the appearance of ordinary connective tissue, the presence of stellate bodies which apparently anastomose together (*vide* fig. 208). In the refractive trabeculæ these bodies seem larger and more defined in outline. This is all we know of the histology of this singular tissue.

When **rachitis is very advanced**, delicate nested lamellæ are found beneath the osteoid tissue. They form perfect cylinders round the bone, and are separated from one another by a soft and vascular connective tissue. These lamellæ, which are formed of true osseous tissue, are themselves cancellous in structure, and the cavities they contain are filled with young connective tissue. This singular development results from fibrous transformation of the old medulla with partial absorption of the bone already formed, and also from incomplete sub-periosteal ossification. As the disease progresses the medulla of the Haversian canals undergoes fibrous change throughout the whole thickness of the compact tissue of the diaphysis; at the same time the osseous trabeculæ are absorbed, and the liberated bone cells mix with the medulla cells. A bone which has undergone these later modifications has partly lost its power of resistance; it may bend under the weight of the body, and be incompletely or completely fractured with the greatest facility.

In fracture of rachitic bone the callus is entirely composed of osteoid tissue, similar to that formed under the periosteum, and there is no cartilage. The callus of osteoid tissue is generally very large. It is not necessary to insist upon the importance of this accidental new formation, which is identical to that produced under the periosteum in the natural course of the disease. In rachitis we have seen calluses which were then old, but produced whilst the disease was still in progress, and they were composed of osteoid tissue without the formation of true bone.

The histological phenomena which take place in rachitic bone during the process of cure are, at present, unknown. It is affirmed that recovery takes place by simply supplying the organism with calcareous salts; but this is a hypothesis which does not rest on any histological data, and which is not in harmony with what is known concerning the process of physiological ossification.

IX. Syphilitic Lesions of the Bones in the New-born.

In 1865 we described the separation of the epiphyses in new-born syphilitic children, and the histological lesions. In 1869 Wegner completed this research, and it has since been extended by Parrot.

Separation of the epiphyses.—In syphilitic children, during the first months of life, complete separation of the epiphyses is often seen at the line of ossification; this generally occurs without the fibrous envelope of the bone (the perichondrium, periosteum, arciform fibres) suffering any solution of continuity. In the cases of separation of the epiphyses observed by ourselves, we found that in sections made parallel to the axis of the bone the ossiform tissue, which normally only forms a thin layer, was much thickened, and that it was composed of directing trabeculæ of cartilage infiltrated with calcareous salts, without there being any formation of true osseous tissue. It is hence conceivable that at this level the friability of the bone would be the greater the thicker the layer formed of cartilaginous trabeculæ, and that separation might be caused by the movements or the weight of the body.

Such, it appears to us, is the true cause of these fractures. Wegner, in a more recent work, maintains a different theory. He thinks that the initial morbid process consists in an exaggerated calcareous infiltration of the cartilage undergoing ossification, which infiltration causes the death of the invaded parts; these acting as foreign bodies on the neighbouring living tissues induce inflammation, the result of which is that embryonic tissue is formed, and the bone partially absorbed, which process leads to a solution of continuity and separation of the epiphyses. Wegner's explanation is similar to that which we gave in describing the phenomena of caries. We still think, however, that our early interpretation is the correct one. We maintain that the initial phenomenon consists in an arrest of the process of ossification, and in considerable thickening of the ossiform layer; the fracture which occurs is the result of an injury falling on that part where the resistance is relatively feeble. We may add that the ulterior lesions, the proliferation of the medullary tissue, the thickening and accidental ossification seen at the level of the wedge of ossification, are often consecutive to the fracture. We do not understand, in fact, how calcareous infiltration of cartilage can be the cause of inflammation, since between cartilage and bone there normally exists a layer of calcified cartilage. The fracture is very often a cause of irritation.

Syphilitic osteophytes.—Parrot has, however, pointed out that neoplasms, showing a marked tendency to the formation of osteoid or osseous tissue, are frequent without any separation of the epiphyses. These growths may be developed on flat bones, as those of the skull; they are at first soft, but eventually become the starting-point of true osteophytes or even of large exostoses. Cranial osteophytes and exostoses are certainly the most characteristic lesions of infantile syphilis. Similar alterations of the long bones should be distinguished from rachitis, properly so called, and referred to syphilis. Syphilitic osteomata are composed of perfect or incompletely ossified trabeculæ, which anastomose together, leaving spaces irregular in form and of variable size, which contain a vascular and more or less fibrous medulla. Ultimately the fibrous trabeculæ thicken, the spaces become narrower, and the growth more closely resembles a syphilitic exostosis of the adult.

M. Parrot admits that syphilitic lesions of the bones of new-born infants are originally distinct from those of rachitis, but contends that they may at a later period assume similar characters. The question of the relation, analogy, and difference between infantile syphilis and rachitis is still surrounded with much obscurity.

CHAPTER II.

LESIONS OF CARTILAGINOUS TISSUE.

Cartilage is a living tissue capable of undergoing primary changes. In the adult, it normally contains no blood-vessels, but it can nevertheless suffer from lesions of an irritative nature (*vide* p. 88), as well as those having a nutritive cause, and in which both the cells and the ground substance are affected.

Changes of nutrition affecting the cartilage cells are: *a.* Granulo-fatty degeneration, which must not be confounded with accumulation of fat (adiposity), a condition frequently met with in the cartilage of adults. This granulo-fatty degeneration causes the death of the cellular element of cartilage, so that at the end of the process islets of fatty granules are found in the matrix in the place of the cells. The intermediate ground substance is softened and often cracked, but it contains no fatty granules. This change is primary; it is not related to inflammation, which is in fact characterised in the period of greatest activity by the opposite phenomenon, namely, by the disappearance of the fat contained in the cells. (For fuller details see article on White Swelling.) *b.* Uric infiltration, which commences in the cartilage cells, has been already noticed on p. 81, and will be more fully described when treating of gout.

The changes of nutrition affecting the ground substance are: *c.* Mucoid change, which is observed physiologically in the costal cartilages (*vide* p. 67), and which may accidentally occur in other cartilages; it is generally accompanied with segmentation of the ground substance. *d.* Calcareous change, which contrary to uric change always begins in the cartilage capsules and extends to the ground substance, never invades the cells. *e.* Finally, uric infiltration of the matrix, which, starting from the cartilage cells, extends into the ground substance in the form of acicular crystals of urate of sodium.

The **irritative lesions of cartilage** are shown by changes which occur simultaneously in the cells, capsules, and matrix. Generally when cartilage cells divide they secrete new capsules around themselves, but sometimes the new cells have lost the property of secreting capsules, in which case they remain in an embryonic condition. This occurs when the irritation is very intense, or when it is associated with calcareous change. The embryonic cells resulting from proliferation either remain as such without changing character, or they become the starting-point of a new osseous or fibrous formation. The irritative lesions of cartilage resemble, in all that is essential, the physiological changes in cartilage near points of ossification: *i.e.* division of the cells, formation of secondary capsules, segmentation and softening of the matrix. The phenomena and lesions vary in the same cartilage—the cartilage of a diarthrodal articulation for example—according to their situation under the perichondrium or on the free part of the cartilage: these are described under acute and chronic arthritis. When cartilages are entirely covered by a fibrous membrane, as the cartilages of the larynx, the costal cartilages, and the intervertebral disks, the cells multiply and secrete secondary capsules around themselves, the irritation frequently ending in true ossification. This is particularly observed in the thyroid cartilage of young subjects affected for several years with phthisis; the ossification is physiological. Some cartilages, if they are subject to a subacute though continuous irritation, finally undergo ossification. This is an extremely curious point in the inflammation of cartilage, and is explained by the close relationship which exists between cartilaginous and osseous tissues, supported by the fact that the primitive skeleton is formed of cartilage.

Ossification of cartilage.—The facility with which proliferating cartilage undergoes ossification enables us to understand how it is that in fractures of the costal cartilages the callus is frequently entirely osseous. We may observe that in fracture of the costal cartilages the irritation present at the extremities of the fragment causes the inflammatory changes described above; the ground substance becomes infiltrated with calcareous salts, the primary capsules enlarge and intercommunicate, the cells become free in the midst of cavities formed of medulla, and ossification proceeds according to the physiological type. We have seen a specimen presented to the Anatomical Society, in which the osseous tissue of the callus was seen to be produced in a very definite manner from the cartilaginous tissue of the fragments. It is extremely remarkable that osseous tissue should be formed in fractures of the cartilages, for in sub-perichondrial resections with the formation of a wound,

M. Peyraud always obtained cartilaginous union. Suppuration of the wound extending even to the seat of resection did not prevent consolidation occurring by means of the perichondrium, which had been preserved; showing that a suppurating wound does not absolutely prevent the new formation of cartilaginous tissue any more than it does osseous tissue in compound fracture.

Ecchondroses.—Cartilaginous tumours may be developed from pre-existing cartilage. On account of their unimportance and slow development they are quite distinct from chondromata; they are called ecchondroses (*vide* p. 392), and are most frequently seen in arthritis, with which they will be described. Lesions of the diarthrodal cartilages cannot be separated from diseases of the articulations, and will be described with them.

CHAPTER III.

PATHOLOGICAL ANATOMY OF THE ARTICULATIONS.

I. Normal Histology of the Articulations.

Before commencing the anatomical study of joint affections, it would be well to describe in a succinct manner the structure of the constituent parts of an articulation in the normal condition.

The cartilages.—The cavities of diarthrodal articulations are bounded by the surfaces of the cartilages, and by the synovial membrane. The elements of diarthrodal cartilages have a certain fixed arrangement; on dividing these cartilages perpendicularly to their surface a series of superimposed layers are observed, the order of which is always identical. On the free surface, flat lenticular capsules are found inclosing a single cell, beneath them round capsules, also unicellular, and deeper elongated capsules placed perpendicularly to the surface and containing two, three, or more secondary capsules arranged in sequence. These elongated primary capsules form linear series continued to the deepest layer, which is infiltrated with calcareous salts and connects the hyaline cartilage with the osseous tissue. All the cells contained in the capsules of the superficial or middle layers contain granules and even drops of fat. The calcified layer is divided from the hyaline cartilage by a wavy line, which on the side turned towards the bone shows a variety of depressions and projections corresponding to papilliform projections of bone which fit into them. In the centre of each of these osseous papillæ there is a medullary and vascular cavity in connection with the cancellous tissue of the bone. It is thus seen that if the plasma of the blood-vessels of the bone reaches the hyaline cartilage, it must do so by traversing the osseous layers and the layer of calcified cartilage. Now, the latter layer contains no canals and does not appear to be permeable, so that the nutritive materials must reach the cartilage in another way; they are very probably obtained from the fluid which bathes the articular surfaces, and which is exuded from the blood-vessels of the synovial membrane.

The synovial membrane.—Structurally the synovial membrane presents both smooth and villous surfaces for consideration. Where the surface is smooth the membrane is composed of a layer of fibrous tissue interspersed with numerous elastic fibres; it is continuous with the peri-articular connective tissue, and is lined with a single layer of epithelial cells. The villous edges called the synovial fringes are particularly seen at those points where the membrane forms folds in passing from one surface to another. They are formed at their bases of two leaflets of synovial membrane brought together in the same way as two layers of peritoneum to form the mysentery. Between the two leaflets are found loose connective tissue, groups of fat cells, and numerous blood-vessels. Owing to their delicacy and transparency these fringes may be studied microscopically by simply cutting them off with scissors. If the blood-vessels are slightly congested, the large size of the veins and arteries cannot fail to be remarked, considering the small amount of tissue they seem to supply; the capillaries form a rich plexus at the free end of the fringes. From this extremity also spring variously formed bodies which have been described by Kölliker; sometimes they are filiform processes formed of an axis of connective tissue covered by two or three layers of epithelium, the cells of which are furnished with processes and contain nuclei bordered by a double line. This epithelium is very similar to that of the buds of the choroid plexus. Sometimes these processes are club-shaped, covered with a similar layer of epithelium; their axis, which is composed of connective tissue, frequently contains cartilage capsules. These different processes do not contain blood-vessels; at their base, which is generally hollowed out and continuous with the synovial fringe, one or more vascular loops are met with. The physiological functions of the synovial fringes seem to us to be very important; the cells which line the filiform or club-shaped processes are the organs which secrete the synovia, and the large and numerous blood-vessels which are present in the fringes convey the materials for secretion. The synovial membrane does not line the surface of diarthrodal cartilages at the points where these cartilages glide over each other. The synovia is a very complex fluid containing albumen, a large proportion of mucin, and a small amount of fatty matters which appear, under the microscope, in the form of granules or droplets; it also contains epithelial and lymph cells. It is important for the pathologist to know the normal composition of synovia, if he would understand its modifications in articular diseases.

Histological lesions of the articulations have been very incompletely studied. Some researches made by Redfern, O. Weber, etc., have revealed certain changes in the articular cartilage, without establishing any anatomical classification corresponding to diseases which are clinically well defined. Thus, according to these authors, the same lesions are met with in white swelling as in every other form of chronic arthritis. Acute rheumatic arthritis was not studied before one of us, in conjunction with A. Ollivier, undertook a research on the subject. In the following description we undertake to show that in the different kinds of arthritis there are not only different lesions, but a peculiar evolution of these lesions. We divide arthritis into acute, chronic, scrofulous (or white swelling), and gouty.

II. Acute Arthritis.

A. Simple acute arthritis and rheumatic arthritis.—Traumatic arthritis in man probably presents the same histological lesions as rheumatic arthritis; in fact the anatomical changes in the latter do not differ from those of traumatic arthritis artificially induced in the higher animals.

The changes in the synovia and synovial membrane.—On opening an inflamed joint a viscid ropy fluid is exuded, the quantity and appearance of which vary according to the degree and duration of the inflammation. In some cases this fluid resembles normal synovia, though more abundant. Like synovia, it coagulates on the addition of acetic acid; it contains a large number of cellular elements, some of which resemble pus cells, others larger and

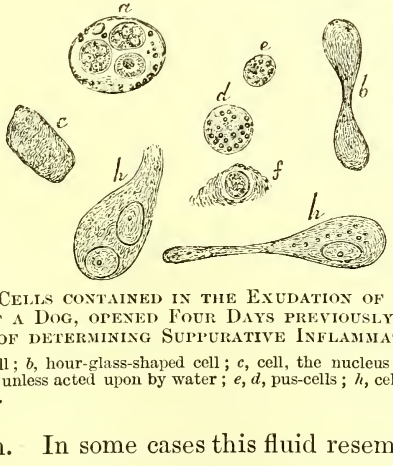

Fig. 207.—Cells contained in the Exudation of the Knee-joint of a Dog, opened Four Days previously with the Object of determining Suppurative Inflammation.

a, mother-cell; *b*, hour-glass-shaped cell; *c*, cell, the nucleus of which is not visible unless acted upon by water; *e*, *d*, pus-cells; *h*, cell containing two nuclei.

rounder contain one or more vesicular nuclei. The protoplasm of these cells usually contains fat granules, which are sometimes very abundant, giving the cell the appearance of a granular body. The synovia is more or less cloudy according to the number of the cellular elements it contains, and the amount of fatty change they have undergone: flakes of mucus resembling sputa are generally seen in the synovial fluid; these flakes are either transparent or more or less opaque, and show all the intermediate stages between mucous and purulent sputa; sometimes, however, they are firmer and are easily dilacerated. On examining minute fragments of these flakes microscopically, the cellular elements described above are seen contained in a granular or fibrillar mass

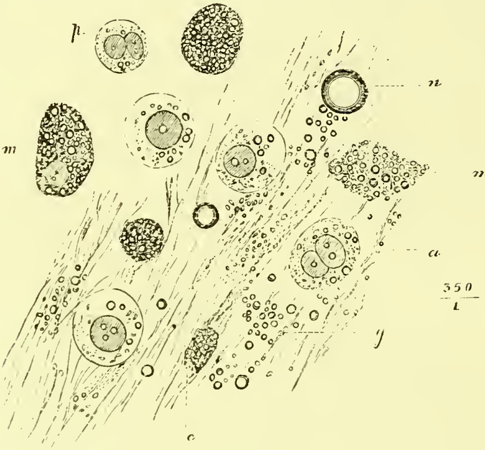

FIG. 208.—MUCOUS OR FIBRINOUS FLAKES OF THE SYNOVIAL FLUID IN ACUTE ARTICULAR RHEUMATISM.

a, large cell; *m*, granular body resulting from cellular fatty degeneration; *n*, free fat droplets; *p*, globule resembling a pus-cell; *g*, fibrinous reticulum including cells and fat granules.

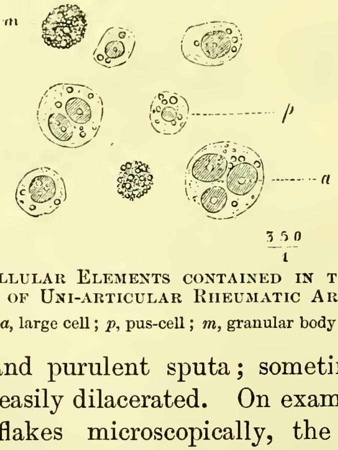

FIG. 209.—CELLULAR ELEMENTS CONTAINED IN THE PURULENT SYNOVIA OF UNI-ARTICULAR RHEUMATIC ARTHRITIS.

a, large cell; *p*, pus-cell; *m*, granular body.

(fig. 208); the more or less puriform appearance of the flakes is in direct relation with the number of cells they contain.

In certain cases of acute rheumatism in which the inflammation attacks a number of small joints, sometimes, however, only one, the articulation is filled with a creamy pus similar to that of an acute abscess; the synovial membrane is injected, the capillaries dilated in an ampullar or fusiform manner, and the cells of the synovial fringes show evident signs of multiplication, their nuclei become vesicular and show one or more brilliant nucleoli. The nuclei are seen undergoing division, and some cells contain as many as ten or twelve nuclei. In a dog, in which acute arthritis had been artificially induced, these cells had the appearance of homogeneous or granular blocks, in which no nuclei were visible before the addition of water or weak acetic acid. In acute articular rheumatism in man, twenty-four hours after death, the epithelial cells of the synovial fringes are much more transparent, the nuclei are visible without reagents, and around them fat granules or droplets of mucin are always present; in man, these cells are always spherical, they may attain a great size, ·02 to ·03 mm. in diameter; their vesicular nuclei and their round and refractive nucleoli give them the size and appearance formerly considered characteristic of cancer cells. In induced arthritis in the dog, cells may be seen with an attenuated extremity by which they ae attached to the surface of the synovial membrane. The connective and cellulo-adipose tissues of the synovial membrane are not generally much modified in this form of arthritis; but if the inflammation lasts long, the lesions of inflamed connective tissue may be observed.

The synovial membrane is not the only part of the joint which becomes diseased in acute arthritis; even in slight rheumatic affections modifications of the diarthrodal cartilages are constantly met with; hence we object to the words synovitis and arthromeningitis introduced by Volkmann, considering that in acute articular inflammation the synovial membrane is not the only part affected.

Lesions of the cartilages.—The lesions which are constant in cartilage are hypertrophy and proliferation of the cartilage cells, which changes are easily recognised, as the cells and capsules have a very regular arrangement in diarthrodal cartilages. On examining a section cut perpendicularly to the surface of the cartilage, the superficial lenticular capsules, which normally contain rather indistinct cellular elements (*vide* p. 379), are the first to be influenced by the inflammatory irritation. The protoplasm of these cells swell, the nuclei themselves increase in volume and become vesicular, a nucleolus becomes distinctly apparent, and the capsules which were flat take a globular form. The various phases of this process can be easily observed in vertical sections cut in the fresh state after treatment with a concentrated solution of picric acid. The following method is preferable, and is that which we recommend, particularly if it is desired to make permanent preparations. Flakes of cartilage separated from the subjacent bone should be immersed for twenty-four hours in a concentrated solution of picric acid. Sections are then cut perpendicularly to the surface, and are placed for twenty-four hours in a solution of purpurin; they are then washed in water and mounted in glycerine. By this method the division of the nucleus involving the segmentation of the protoplasm may be followed. At a given moment the capsule may contain several cells, but soon each cell surrounds itself with a secondary capsule, so that the lenticular capsules on the surface, which physiologically contain only one cell, now contain two or more secondary capsules which have become globular. We may observe that most authors, who have observed this phenomenon (Redfern, O. Weber, etc.) in chronic arthritis only, have mistaken the secondary capsules for cells. This mistake cannot occur if a solution of iodine be used, which stains the protoplasm of the cells brown, leaving the secondary capsules of a very pale tint. This multiplication of the superficial cellular elements does not generally extend throughout the whole of the cartilage, but occurs in disseminated spots. This is a constant fact of which we can at present give no explanation. The same irregular distribution of the morbid process is met with in the deep layers, which may also be affected if the arthritis is intense and of long duration.

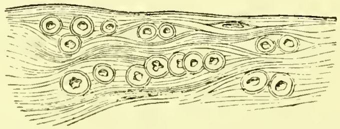

Fig. 210.—Surface of the Condyle of the Femur in Acute Articular Rheumatism.

The superficial capsules contain secondary capsules which themselves contain cells. Magnified 200 diameters.

When the deep layers are affected, the cartilage shows changes which are appreciable without the aid of the microscope. These consist in slight tumefactions which cease to give the finger the feel of resistance peculiar to cartilage, and into which the point of the scalpel penetrates easily. Villi formed by slitting of the cartilage and pressed together are often seen on these tumefactions, or shreds many millimetres in length free at one end and adherent by the other. In acute uni-articular arthritis, ulceration of the cartilage may be sometimes observed, differing from that of white swelling and chronic arthritis, but causing erosions resulting from the rapid melting of the cartilaginous substance. In a section cut at right angles to the surface of the cartilage at the points where it is tumefied, an active proliferation of the deep layers and even of the calcified layer is seen to have taken place. In the multiplication of the cells and the formation of secondary capsules, the process does not differ from that described in the superficial layers; only as the primary capsules of the middle layer are arranged in linear series and are pressed together, they elongate so as to form rows perpendicular to the surface of the cartilage, while the superficial lenticular capsules filled with secondary capsules form lines which are parallel to the surface. As proliferation is always accompanied with splitting up of the matrix, this segmentation gives the appearance of striæ, parallel to the long axis of the primary capsules (*vide* figs. 210 and 211), from which it results that in the deep layers this segmentation is at right angles to the surface, while in the superficial layers it is parallel. When the morbid process is very advanced, the striæ give origin to clefts which divide the diseased cartilage, just as if incisions had been made with a knife. These divisions are parallel to the surface in the superficial layers, and perpendicular to it in the deep layers. This decomposition of cartilage, which might be mistaken for the villous state of chronic rheumatism, differs from it in a marked degree, as we shall see later on; we call this state the pseudo-villous. Flakes parallel or oblique to the surface may be detached by these incisions. They are often longer than the entire thick-

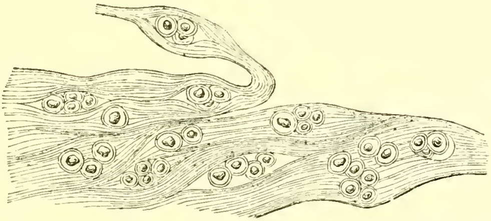

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FIG. 211.—SURFACE OF THE CONDYLE OF THE FEMUR IN ACUTE ARTICULAR RHEUMATISM.

Oblique segmentation of the cartilage; a layer raised containing a primary capsule, in which there are many secondary capsules. Magnified 200 diameters.

ness of the cartilage, and they often contain proliferating cellular elements. If there is positive ulceration of the cartilage, the matrix softens, undergoes a kind of liquefaction, and the proliferated cells become free.

From what precedes it is seen that in acute arthritis the diarthrodal cartilages are affected as well as the synovial membrane; the lesions being produced in both simultaneously. It cannot be denied, however, that hyperæmia and exudation, the starting-point of which is in the blood-vessels, play an important part in the inflammatory lesions of cartilage; indeed, we have seen that the superficial cells of the latter are the first affected, and their initial lesions must be attributed to the fact that they are in direct relation with the exuded fluids from which they draw the materials of nutrition. We have shown, in fact, that cartilage does not draw its nutritive fluids from the blood-vessels of the bone, since this is prevented by the calcified layer; the cellular elements have notwithstanding an individual activity in arthritis, for although all are equally moistened by the fluid, all do not equally undergo proliferation. This is a very important fact, on which we insist, for there are certain pathologists who deny cells all formative activity in inflammation.

B. **Purulent arthritis.**—By purulent arthritis we do not mean suppurative inflammation such as is met with in acute rheumatism, traumatic arthritis, or suppurating white swelling, but simply the rapid and abundant formation of pus in a joint, a suppuration which is not proportionate to the other inflammatory phenomena. This form of arthritis is met with in purulent infection, puerperal fever, malignant smallpox, glanders, etc. The synovial membrane and fringes are more or less affected; in the cartilages morbid appearances are not detected with the naked eye. The dominant lesion consists in a considerable quantity of pus such as is met with in an abscess. It is evident that this rapid and excessive production of pus cells cannot be explained by simple epithelial proliferation; diapedesis gives an explanation, though it is still difficult to understand how so large a number of pus cells can be derived from the blood since, in purulent arthritis, many articulations may be affected at the same time, and similar inflammatory lesions may exist in other organs.

In a few cases of purulent arthritis we have observed more or less advanced lesions of the diarthrodal cartilages. In one case, due to purulent infection, the cartilaginous covering had almost entirely disappeared, a small part only of one of the condyles of the femur being covered with cartilage; all the rest of the bony surfaces of the joint were covered with a calcified layer. In transverse sections of this remnant of cartilage (cut after maceration in Müller's fluid) it was distinctly seen how the cartilage had disappeared, and how its cellular elements had been directly changed into pus cells. The primary capsules were elongated (*a*, fig. 212), and filled with free cells, the secondary capsules having been dissolved, and they formed long rows either perpendicular or aslant to the articular surface. The most superficial of the rows of cells opened into a purulent mass (P), the constituent cellular elements of which did not differ from themselves, both being of the same size, of round or irregular form, filled with flat granules; some even were converted into granular bodies. It is evident that all the pus cells in a joint in purulent arthritis are not derived from the cartilages, but it is none the less certain that a great number originate there.

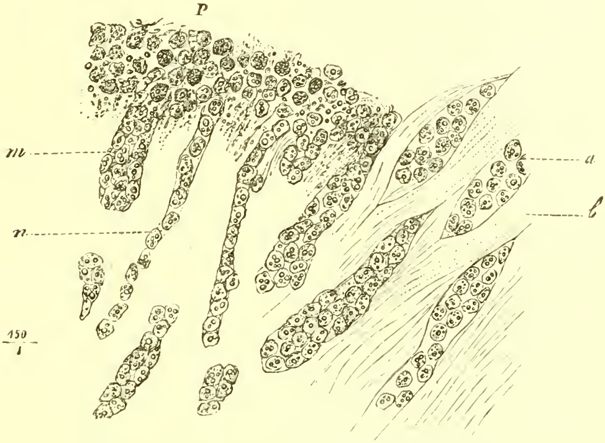

FIG. 212.—ARTHRITIS OF PURULENT INFECTION.

a, primary capsule filled with free cells; *b*, segmented matrix; *m*, primary capsule opening on to the surface; *n*, capsule similar to the preceding, in which the free cells are arranged one after the other; P, purulent layer on the surface of the cartilage.

III. Chronic Arthritis.

A. **Hydarthrosis.**—There is a division of opinion as to the place hydarthrosis should occupy in the classification of diseases of the articulations: some observers, such as Blandin, Bonnet, Billroth, and Volkmann, include it among inflammatory lesions;

others, such as Dupuytren and Nélaton, look upon it as a hydropsy. This disagreement is owing to the variety of articular affections called by the name of hydarthrosis. Indeed, on studying the reports of autopsies, among others those made by Dupuytren, Blandin, Brodie, and Bonnet, it is seen that in diseased joints the lesions of acute or chronic rheumatism may be sometimes found, such as congestion, thickening of the synovial membrane, hypertrophy of the fringes, and even ulceration of the cartilages; while in other cases there are on the contrary no lesions appreciable to the naked eye, the synovial membrane is smooth, and looks only as if it had been washed (Dupuytren). Patients affected with hydarthrosis do not die except from some intercurrent accident; the opportunities therefore of studying the lesions of hydarthrosis are very rare, and we believe that hitherto no histological examination has been made, except of the fluid obtained by puncture. In this, epithelial cells, clear or filled with fat granules, have been found (Volkmann), but these elements are also met with in normal synovia, and hence we learn nothing positive regarding the nature of the lesion from their presence.

B. **Chronic arthritis by continuity of the inflammation.**—This form of arthritis is very common. It is important from the fact that the investing cartilage is affected in a marked degree, while the synovial membrane presents no appreciable lesion. It occurs in joints situated at the extremities of a bone affected with inflammation or a rapidly growing tumour (sarcoma, carcinoma, etc.). When an articulation is in a state of suppurative inflammation, as is observed in the second period of white swelling, and the corresponding bones are affected, the neighbouring joints present the following lesions: the articular cavity contains no more fluid than normally; the synovial membrane is generally slightly hyperæmic, though the fringes may show marked congestion; the cartilages, principally those in relation with the diseased bone, are more or less deeply eroded, and the denuded surfaces are covered with a layer of new connective tissue. These erosions are generally irregular in shape and variable in extent; they are usually found at the periphery of the cartilage, and they may extend to the edge of the synovial membrane. Very often, however, solitary or confluent erosions may be observed in the centre of the cartilage. The peripheral losses of cartilage are often replaced by a vascular connective tissue which is continuous with the synovial membrane, but if they occur in the centre of the cartilage they have a denuded appearance, and seem to be replaced by a non-vascular soft mass. Transverse sections of these eroded portions of cartilage show that the loss of substance is due to the solution of the cartilage by proliferation of the cellular elements; this occurs slowly, layer by layer, so that the capsules near the ulcerated spot only show phenomena of proliferation similar to those seen in acute arthritis. The edges and base of the eroded spot are notched, each notch corresponding to an opened primary capsule, the cells of which have escaped and mixed with the synovia, or else have remained *in situ* to help to form the mass of embryonic cells which fill up the eroded cavity. These cells may form embryonic connective tissue, particularly when the erosions are related to the connective tissue of the synovial membrane; the blood-vessels of the latter are pushed out and form loops which gradually advance into the midst of the embryonic connective tissue.

Vascular development can be well studied in these blood-vessels, for they are located in so thin a structure that the layer can be submitted entire to microscopical examination. The membrane should be placed in a saturated solution of picric acid and mounted in glycerine. The vascular loops are then seen to spring from the synovial membrane, in the same way as in keratitis the blood-vessels of the conjunctiva advance towards the cornea. The capillaries of these loops vary in size; some are so fine that they cannot contain a blood corpuscle, while others are on the contrary dilated in a regular, fusiform, or ampullar manner; the latter is rare. From the convex side of the loops very delicate canals are seen to spring; they contain red blood corpuscles, and seem to be lost in the tissues; but it is possible that they are far-extending portions of loops, part of which has escaped observation. This system of superimposed arcs recalls the arrangement of the blood-vessels in the mesentery. The minute histological changes which result in the formation of the blood-vessels have not been made out.

In this form of arthritis it is rare for the inflammation to be so intense as to cause suppuration. It is, however, seen in acute suppurative ostitis, in which the bone is absorbed and replaced by granulations. The cartilage also disappears, the calcified layer alone remaining. This is chiefly observed in diffuse phlegmonous ostitis, in deep-seated whitlow, and in a certain form of destructive ostitis of the phalanges which accompanies perforating ulcer of the foot.

C. **Chronic rheumatic arthritis.**—This is also called deformative,

formative, or proliferating arthritis, nodular rheumatism, and *morbus coxæ senilis.* Though the names nodular rheumatism, dry arthritis, and *morbus coxæ senilis* represent distinct clinical varieties, it is nevertheless true that the anatomical lesions and their evolution are the same in these different diseases. They are essentially characterised by a villous condition of the cartilages, by hypertrophy of the synovial fringes, and by ecchondroses or osteophytes at the edges of the articular cartilages; these serious lesions are not accompanied by any marked effusion into the articular cavities. They differ also according to the articulations diseased, and the period of the disease. In the articulations of the phalanges, for example, the changes consist in the gradual disappearance of the centre of the cartilage by villous change, to be presently described, and afterwards in the development of small nodules of cartilage (ecchondroses) on the borders of the cartilaginous investment of the joint. These ecchondroses give the finger joints the peculiar appearance which has given the disease the name of *nodular rheumatism.* At a later stage, the centre of the cartilages disappears, and the ecchondroses ossify, and the articular surfaces, which are formed of eburnated bone, lose their original form, and become covered with lines and grooves, the direction of which is determined by the articular movements. In the large articulations, of which the knee may be taken as the type, there is seen the same disappearance of the cartilage at the centre, and the same production of marginal ecchondroses; but the synovial fringes and interarticular ligaments also undergo considerable changes. The fringes hypertrophy, their villi bud and give off secondary villi, producing what has been called the *dendritic or arborescent budding of the synovial membrane*; a considerable development of blood-vessels accompanies these new growths. The synovial buds generally become cartilaginous and form spherical or ovoid masses of different sizes; they may be as large as a hazel nut and be retained by a very fine pedicle, which may break when the mass becoming free forms a foreign body in the joint. Sometimes these cartilaginous growths become infiltrated with calcareous salts, and present both the gross and microscopic appearances of vascularised bone. In such articulations also there is considerable hypertrophy of the interarticular ligaments, so that they resemble cartilage.

Changes in the cartilages. Villous change.—Whatever may be the articulation attacked, the histological process is the same in all forms of the disease; it consists essentially in proliferation of the cartilage and a new formation of cartilage in the fibrous parts, whence the term which defines the disease best is that of proliferating arthritis. The histological lesions of chronic rheumatism have been studied by Redfern, O. Weber, Volkmann, etc.; they described the lesions at the centre of the articular cartilage which produce the villous state; but they did not appreciate the changes in the periphery which result in the formation of ecchondroses. In sections cut perpendicularly to its surface the cartilage shows throughout its whole extent, as far as its borders, multiplication of the cartilage cells, with formation of capsules around themselves; the enlarged primary capsules contain a great number of secondary capsules; more often the secondary capsules form groups enveloped in a common capsule, these groups being included within the primary capsule; in other cases the primary capsules are filled with small round capsules unconnected with one another. Previous observers have mistaken these round capsules for true cells; this is an error against which we have long contended, and which may be avoided by employing a solution of iodine which stains the protoplasm of the cells brown and leaves the secondary capsules colourless or very slightly tinted. The primary capsules on the surface become globular and distended, when they rupture and open on to the articular surface. The second row of capsules and those which are more deeply seated cannot enlarge except perpendicularly to the surface of the cartilage; as they are arranged in linear series they open into one another, and form, as it were, parallel tubes filled with cells. These phenomena are similar to those observed in cartilage near a centre of ossifi-

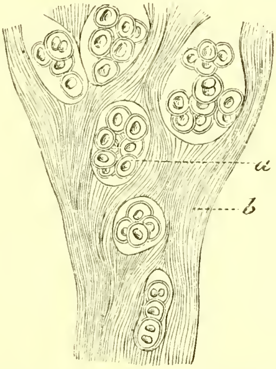

FIG. 213.—NODULAR RHEUMATISM.

Surface of the cartilage; *a*, primary capsule filled with secondary capsules about to open into the articulation; *b*, segmented matrix. Magnified 200 diameters.

cation (*vide* p. 22). The superficial, enlarged, primary capsules gradually discharge their contents into the articular cavity, and the grooves which formerly lodged the cells are left filled with synovia or cellular debris. The matrix between these emptied spaces persists for a long time in the form of long or short villi floating at the free end of the cartilage. These filaments are generally very delicate; they may be formed simply of ground substance, or they may contain a few cartilage capsules, which are generally to be found at the free end of those villi which are club-shaped. The villi may attain and even exceed 1 mm. in length. They are perpendicular or more or less obliquely inclined to the surface of the cartilage; swellings may be seen here and there in which are located primary capsules. As the disease progresses, the cartilaginous villi, deprived of their cells and subjected to the friction of the articular surfaces, gradually disappear as far as the calcified layer; this is in its turn eroded, the subjacent bone undergoes eburnation, and may be also eroded by the articular movements.

Ecchondroses.—Ecchondroses are not characteristic of chronic rheumatism; they are sometimes met with in other forms of arthritis of slow development, due to scrofula or gout; in fact, when ever the borders of an investing cartilage undergo rapid proliferation, nodosities are formed, the centre of the cartilage constantly disappearing at the same time by splitting up into villi. Thus the curious phenomenon may be seen of the same disease causing on the same articular surface the disappearance of a large part of the investing cartilage, while it simultaneously produces an exuberant formation of cartilage; the two lesions are nevertheless caused by an identical histological process; the difference results from the borders of the articular cartilage being covered by the synovial membrane, under which the proliferating elements accumulate instead of being discharged into the articular cavity. A transverse section shows first a fibrous membrane, succeeded by fibro-cartilaginous tissue, and finally by proliferating hyaline cartilage. The fibrous membrane, which is in some cases distinctly vascular, varies in thickness, and is directly continuous with the synovial membrane and the periosteum; beneath it is a fibro-cartilaginous layer by which it is united to the hyaline cartilage; in the latter are found large capsules with secondary capsules forming complicated systems. This tissue closely resembles the cartilaginous layers which precede ossification of the short bones. Our explanation of the formation of ecchondroses differs from that which has been hitherto given. It was formerly thought that as friction of the articular surfaces plays a considerable part in the disappearance of the centre of the cartilages, and inasmuch as the periphery of the cartilage is not subjected to this friction, it is here that proliferation necessarily causes an accumulation of cartilaginous tissue. This explanation is invalidated by the fact that ecchondroses are always covered by the fibrous tissue of the synovial membrane, beneath which the proliferating elements are imprisoned and accumulated. In the same way, any part of the articular cartilages which is covered by the fibrous tissue of the synovial membrane may give rise to nodosities; for instance, the synovial fringes and the tendons and ligaments, particularly at their points of insertion.

Osteophytes.—Ecchondroses finally undergo ossification, the process is normal and always commences at their bases, near the parent bone. The osseous tissue gradually encroaches upon the ecchondrosis till it finally disappears to give place to a cancellous or eburnated osteophyte. In chronic rheumatism osteophytes are generally eburnated superficially, while their deeper layers are cancellous, and contain adipose medullary tissue, as in the rest of the head of the bone. The limit between the old and the new bone is well marked. Osteophytes in fact resemble epiphyseal exostòses. They are of very varied forms, and sometimes of enormous size. The most remarkable examples of this variety of osteophyte are seen in the hip joint in *morbus coxæ senilis*, a form of dry arthritis. The osteophytes developed round the femur increase on the side of the trochanter major so that the head of the bone becomes of an enormous size, while the neck seems to have disappeared; similar osteophytes are at the same time found all round the acetabulum, by which new growths the capacity of the cavity is increased to correspond with the increased size of the head of the femur. Nothing can be more irregular than the form and size of these osteophytes. All the tendinous insertions near an articulation may become the starting-point for the formation of osteophytes, and when such is the case the diseased joint is deformed in the most singular manner.

Changes in the bones. Eburnation.—As we have already indicated (p. 392), the head of the bone becomes eburnated after the disappearance of its cartilaginous covering, which is brought about by splitting up of the cartilage into villi and its subsequent erosion. This is seen particularly in the chronic arthritis of locomotor ataxy. This form of arthritis, which was discovered by Charcot, is peculiar in that it gives rise to extremely rapid erosion of the heads of long bones; in the shoulder joint, for example, Charcot has seen cases in which the head of the humerus had completely disappeared. The cause of this superficial eburnation is a point not easily determined: we have, however, observed some facts which may explain the process. While the superficial capsules of the cartilage become filled with new cellular elements, those which, more deeply seated, are in relation with the calcified layer undergo similar changes; in enlarging they approach the bone and bring about the absorption of the calcified layer; the osseous trabeculæ which separate them from the medullary cavities are absorbed by a process similar to that observed in ostitis, and the enlarged capsules finally open into the medullary spaces of the bone, into which they discharge the cells they contain; whence it follows that the medullary spaces adjoining a cartilage of investment are filled with newly formed cells derived from the cartilage, and which have all the characters of the elements of embryonic medulla. The sub-cartilaginous osseous layer which contains this embryonic medulla is thin and has the appearance of a red line; the eburnated layer is derived from this by the successive conversion of the embryonic cells into bone corpuscles by the normal process of ossification. It is probable, however, that the sub-cartilaginous layer of compact bone is not always produced by this process; it is possible that the in-

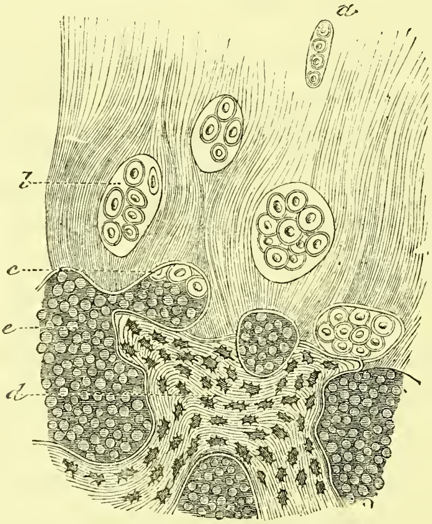

Fig. 214.—Nodular Rheumatism.

Deep layer of cartilage: *a*, normal capsule; *b*, mother capsule containing secondary capsules; *c*, capsule emptying its contents into a medullary space; *d*, osseous tissue of new formation; *e*, embryonic medulla. Magnified 300 diameters.

flammation may extend in a direct manner to the cancellous tissue, and there determine inflammatory eburnation. In all the other parts of the epiphysis the medulla is adipose, and the excess of fat may be so great, and the osseous trabeculæ thinned to such an extent, that they may be easily broken down by the finger pushed deeply into the spongy tissue. These thinned osseous trabeculæ, examined microscopically, are found to be quite regular, and show lacunæ filled with bone cells containing no fat granules.

Changes in the synovial membrane.—The synovial fringes become vascular, the adipose tissue which they contain disappears, and is replaced by embryonic cells, which by accumulating produce the secondary arborescent growths already described (p. 390); some of the embryonic cells contained in the buds form cartilage, while those at the periphery form a continuous layer of fibrous tissue. The nodules of cartilage thus produced may be numerous though small; those which are located at the base of the fringes unite and form thick plates which spread out more or less over the rest of the synovial membrane; others in the villi are connected with the membrane by pedicles varying in length and thickness. This formation of cartilage in the ends of the synovial fringes does not constitute heteroplasia in the sense in which Virchow understands the word, for cartilage capsules are sometimes normally met with in the fringes (Kölliker). These cartilaginous growths may undergo calcareous infiltration or even true ossification; in the latter case the tissue always becomes highly vascular; we have even seen cartilaginous nodules united to the synovial membrane by delicate pedicles which have notwithstanding undergone ossification, but in these cases the pedicle contained blood-vessels. Very often these pedunculated masses, whether cartilaginous, calcified, or ossified, become detached and form foreign bodies in the joint.

Causes of immobility.—It is curious to note that chronic rheumatic arthritis, accompanied by an exuberant formation, first of cartilaginous and then of osseous tissue, does not induce osseous ankylosis, contrary to other forms of chronic arthritis, in which, on the other hand, such considerable osseous growths are not produced. The immobility of the articulations in chronic rheumatism is often due to osteophytes which do not unite; or in very rare cases, to fibro-cartilaginous change of the synovial membrane, or even to fibrous union of the two articular surfaces deprived of their cartilages.

In concluding this description of chronic rheumatic arthritis, it should be added that, in a case of tarsalgia examined by Gosselin, lesions of the cartilages were observed similar to those seen in the first period of chronic rheumatism. (Thèse de Cabot, 1865.)

IV. Scrofulous Arthritis, or White Swelling.

Surgeons have hitherto described 'white swelling' without defining it either from the clinical or anatomical point of view; their descriptions include many species of articular disease; in fact, clinically, they call 'white swelling' all chronic articular affections which suppurate, or show a tendency to suppurate. The puffiness and pallor of the integuments have also formed part of their definition, though they recognised the fact that at certain periods of white swelling the skin and subcutaneous tissue may be the seat of inflammation accompanied with redness. In describing the lesions of joints thus affected, they have included every possible alteration of the synovial membrane, cartilages, and bones. Bonnet is the only author who tried to find a constant anatomical characteristic in white swelling in the existence of fungoid granulations of the synovial membrane and bones. But these fungoid growths are not present at all periods of white swelling, and they present no special anatomical character, as they do not differ essentially from other voluminous granulations which may be developed elsewhere.

In the clinical history of this disease there are generally two stages: the first is long, and is characterised by difficulty of movement or by dull pain; the second is marked by the accidents of suppurative inflammation, which may be very acute. The variety of opinions and the hesitation felt by pathologists regarding this disease are due to the fact that they have not recognised the lesions of the first period of white swelling, and hence they have not understood the *rôle* of these lesions in the production of the accidents of the second period. Such an investigation cannot however be made without the use of the microscope. The anatomical lesions of white swelling differ in the two periods of the disease: in the first period they consist in fatty degeneration of the cartilage cells, and often also of the bone cells of the epiphyses; in the second period the parts destroyed by fatty degeneration determine an eliminative ulceration around themselves (arthritis, rarefying or suppurative ostitis, fungosities of the synovial membrane, caries, necrosis, hyperostosis, abscess, or condensation of the bone, chronic inflammation, or abscess in the neighbouring tissues).

To recapitulate, *the anatomical definition of white swelling is based on its initial lesion, which is fatty degeneration of the cellular elements of the cartilage and bone; all the other lesions are those of inflammation.*

First period.—The lesions of white swelling are very rarely observed in their initial period; we have, however, had the opportunity of seeing two cases; but even when suppurative inflammation has supervened, traces of the primary lesions can be found in the cartilages and bones. In our cases, the synovial membrane did not appear to be much altered, though there was a greater quantity of synovia present in the joint than normally. In one case on the surface of the synovial membrane, as well as on the cartilages, there was a concrete and mucous exudation, greyish and gelatiniform, which in microscopic sections appeared to be formed of a beautiful network, in the meshes of which was found a fluid substance containing no cellular elements (fig. 215). This exudation was adherent to the cartilages; which had nevertheless preserved their polished surfaces, though they were slightly opaque and had lost some of their elasticity. In transverse sections, examined under the microscope, the successive layers described on p. 379 were found, only that the cells contained fine fat granules, some of them being completely destroyed by the fatty degenerative process (A, fig. 215). This began in the superficial layers, and gradually invaded the deeper parts till the whole thickness of the cartilage was affected; there was generally an unequal dissemination of the morbid process, in which peculiarity it did not differ from other cartilaginous lesions; some part of the articular

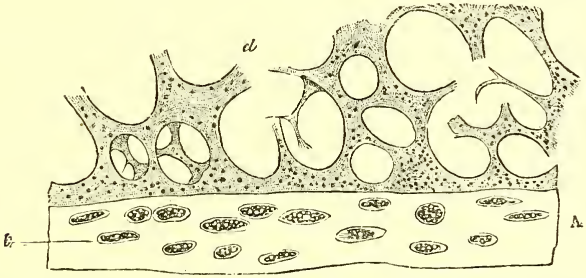

Fig. 215.—Transverse Section of the Articular Cartilage and the Mucous Exudation covering it, from a Case of White Swelling in the First Period.

A, section of the cartilage showing the superficial cells; c, filled with fat granules; B, reticulate mucous exudation.

cartilage having undergone complete change, while others were only modified superficially, or showed no alteration at all.

Fatty degeneration always ends in the destruction of the cells contained in the capsules, so that when complete only fat granules are found in the capsular cavities, the nucleus of the cell having disappeared; at the same time the matrix softens and offers no resistance to articular movements and pressure, so that the capsules containing only fat granules finally become deformed and take the irregular shapes represented at fig. 216. Very often this morbid process is continued in the second period, and sometimes, when the entire cartilage has undergone fatty degeneration, it may remain without undergoing other modifications. In the epiphyses are found the lesions of caries in the first period, that is to say, extreme thinness of the osseous trabeculæ, the corpuscles of which have for the most part undergone fatty degeneration, while the medulla is yellow, adipose, and but slightly vascular. The periosteum and soft parts surrounding the articulation seem to be perfectly healthy.

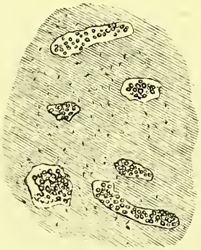

FIG. 216.—SECTION OF ARTICULAR CARTILAGE FROM A CASE OF WHITE SWELLING IN THE FIRST STAGE.

Complete fatty degeneration of the cartilage cells.

Second period.—The lesions of the second period vary according to the duration and intensity of the inflammation consequent on the fatty necrobiosis of the cartilage and bones. The synovial membrane becomes highly vascular and thickened; its adipose tissue disappears to give place to an embryonic tissue which buds and secretes pus which is discharged into the articular cavity. When the disease is more advanced and the cartilages are destroyed, the osseous extremities become covered with granulations which blend with those from the synovial membrane; if the purulent focus opens externally, the fistulous track is also lined with similar granulations. In white swelling these granulations are called **fungosities**. They generally rest on a highly vascular, friable, and semi-transparent layer of granulation tissue, which may become lardaceous in consistency when suppuration ceases and the tissue tends towards a higher organisation; sometimes all the fungosities may undergo caseous degeneration. They vary in structure according to their degree of development. On this subject we have nothing more to add to what we have already said when considering caries, to which chapter we refer the reader (*vide* p. 343).

The changes which the cartilages undergo are not always identical. When the cells have undergone fatty degeneration throughout the whole thickness of the investing cartilage, the latter behaves like an inert body; it softens so that it is detached by the movements of the joint in the form of flakes of variable size, which, attached by one border or perfectly free, float in the articular cavity. The granulations developed on the epiphyses may also raise and detach the cartilage, which then floats free in the pus filling the joint. When the cartilaginous covering has not been affected throughout its whole extent, the elements of the deep layers, which are generally respected, show irritative lesions, which result in partial thickening, ulceration leading to villous change, the formation of fibrous tissue, and even to ecchondroses. The cartilage cells which are the seat of inflammatory phenomena and active new formations do not contain fatty granules. The superficial layer of cartilage having become inert by the destruction of its cells, the capsules of the deep layer, filled with secondary capsules and arranged in rows, cannot consequently open on to the surface of the joint and discharge their contents. Simultaneously

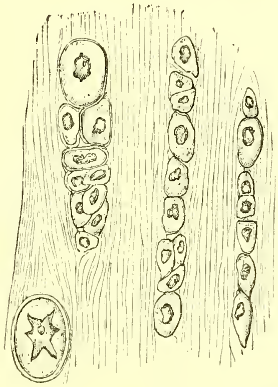

FIG. 217.—WHITE SWELLING; SECOND OR INFLAMMATORY PERIOD.
Elongated mother capsules of the diarthrodal cartilage forming rows of secondary capsules; the matrix is segmented. Magnified 200 diameters.

with this proliferation, the matrix becomes transparent, and splits up parallel with the rows of secondary capsules. This process (fig. 217) produces thickening of the investing cartilage, so that here and there it may attain 7 mm. in thickness. The hypertrophy is generally limited, and side by side with exuberant development of cartilage in disseminated spots may be seen granulations, fibrous tissue in process of organisation, or even ulceration of the surface of the cartilage, leading to the formation of villous filaments resembling in shape and development those of chronic rheumatism. In the second stage of certain cases of white swelling of slow growth, marginal ecchondroses may be observed, less developed and more irregular, it is true, than in chronic rheumatism ; their origin and structure are, however, the same in the two diseases. They are developed under the thickened fibrous tissue which has taken the place of the synovial membrane. Whether the cartilage has been raised in masses by the bone granulations beneath, or has been worn away by villous ulceration, it disappears entirely, and is replaced by granulations or by an embryonic fibrous tissue ; the joint is then transformed into an abscess lined with a pyogenic membrane. When the pus is discharged, the articular cavity becomes lined with large fungoid granulations. The granulations of opposed surfaces touch but become united, so that in the place of an articular cavity there is a continuous layer of embryonic tissue between the two osseous surfaces of the joint. Osseous trabeculæ are developed in this young tissue, and lead to a complete union of the two bones. This is a favourable mode of termination of the disease ; it must however be noted that osseous ankylosis may occur without the cessation of suppuration.

The lesions of the epiphyses in white swelling are those of caries followed by all the accidents of this disease. It is doubtful if true caries is ever developed far from a joint (Volkmann), but it is most frequently accompanied by the articular changes of white swelling. To what has been said regarding caries it must be added that the granulations or fungosities springing from a bone often project into the articular cavity after the partial or total disappearance of the cartilage. The caseous sequestra or small sequestra of caries may also be discharged into the articular cavity.

The lesions of the soft parts surrounding a joint, the connective tissue, the sheaths of the tendons and the tendons themselves, are those of chronic phlegmonous inflammation. It is particularly round the fistulous tracks that inflammatory new formations are seen ; there is no essential difference between these various lesions and those which occur round a necrosed bone ; at the commencement of the second stage, however, thickening of the connective tissue is observed, which will be studied when considering the inflammation of this tissue.

Chronic arthritis, such as we have described, is most frequently seen in subjects who present the clinical sign of a scrofulous diathesis, among whom many are the subject of tuberculosis. In some cases the synovial membrane, the bones, and the fistulous tracks lined with granulations, are also the seat of tubercle. This form of arthritis should be classified apart, and, though insufficiently understood both clinically and anatomically, we have devoted a special article to tumours of the articulations.

V. Gouty Arthritis.

Gouty affections, like scrofulous affections of the articulations, may be divided into two stages. In the first, simply nutritive lesions of the cartilages, synovial membrane, and neighbouring fibrous tissue are present; in the second are observed the inflammatory lesions which are the necessary consequence of the former.

First period.—The lesions of this stage consist in an infiltration of the cartilages, the synovial membrane, the fibrous tissue adjoining the articulation, the subcutaneous serous bursæ, and even the periosteum and the areolæ of the cancellous tissue of the epiphyses with urate of sodium, generally in the form of acicular crystals. In the cartilage the urate of sodium is first deposited in the most superficial part of the articular cartilage, never on its surface, as might be concluded from an examination with the naked eye. It seems, in fact, on examining the articular surface, as if a layer of polished plaster had been extended over it. Though generally shining, this layer is very opaque ; on it may sometimes be distinguished hardly perceptible and irregularly distributed grooves. In a perpendicular section of the cartilage the deposit is seen to occupy only the most superficial part. On making a microscopical examination in water, glycerine, or a neutral fluid, the urate of sodium is very often seen to be accumulated in such large quantities on the surface of the cartilage that only an opaque granular line can be distinguished ; but deeper, at the edges of this layer, acicular crystals can be seen, radiating from a central point, which is generally a cartilage cell. These acicular crystals, which often measure ·05 to ·06 mm. in length, are either rectilinear or slightly curved. It is singular to see such regular crystalline forms produced in a solid medium, such as cartilage; all the more so that the crystals traverse the different elements, the cell, the capsule, and the matrix, exactly as if these were composed of a homogeneous fluid. When the deposit of urates is considerable and numerous crystals radiate from the surface of a cartilage capsule, the latter is opaque and resembles a thorn apple. To ascertain that the black line on the surface of the cartilage is not simply due to an added deposit, it suffices to treat the preparation with acetic acid, or a 40 per cent. solution of potash. The salts are gradually dissolved out, and it is then seen that they were everywhere deposited in the cartilage itself. The solvent reagent acts on each group of crystals from the periphery towards the centre, so that the urates may be entirely dissolved out of the matrix, while the cells remain infiltrated. When acetic acid is used, at the same time that the crystals of urate of sodium disappear may be observed the formation of the lozenge-shaped or hexagonal, transparent, and colourless crystals of uric acid. The connective tissue of the synovial membrane shows small white opaque spots, produced by deposits of urate of sodium; though apparently superficial, these deposits are located in the midst of the fibrous tissue, and cannot be removed by scraping.

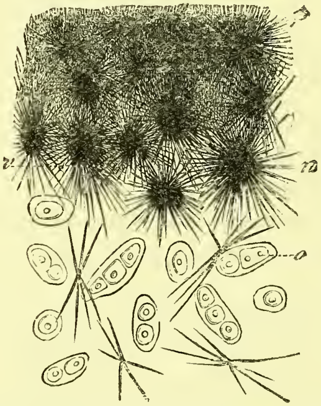

Fig. 218.—Perpendicular Section of an Articular Cartilage infiltrated with Urate of Sodium from a Gouty Subject.

p, articular surface of the cartilage; *v*, *n*, amorphous and acicular urates; *o*, cartilage capsules. Magnified 200 diameters.

Chalk stones.—The synovial fringes, the ligaments, periosteum, sheaths of the tendons, peri-articular connective tissue, sheaths of the nerves, external sheaths of the blood-vessels, and the skin itself may be invaded by deposits of urate of sodium. The salts seem to be deposited between the fibres of the connective tissue, so that the white opaque mass cannot be isolated, and in its substance, besides granules and crystals of urates, are found fibres of connective tissue. When these peri-articular deposits attain such a size that they are recognisable during life, they are called tophi or chalk stones. In the centre of a tophus there is often a white softened chalky mass, on removing which can be seen the wall of the cavity in which it was contained. This wall may be very thick, and is formed of a kind of felting of connective tissue infiltrated with urates. On mixing the soft chalky mass with water, beautiful acicular crystals of urate of sodium are obtained.

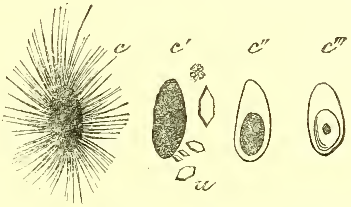

FIG. 219.—SOLUTION OF URATES BY ACETIC ACID.

c, cartilage cell and capsule bristling with acicular crystals; these crystals are the first to disappear, then the amorphous urates, *c′*, *c″*, *c‴*, are gradually dissolved and form uric acid crystals, *u*. Figure partly diagrammatic.

Second period.—In the second period of the disease the cartilages, irritated by the presence of the urate of sodium, undergo changes which may be regarded as inflammatory. This irritation is recognised by a peculiar appearance of the deep layer of cartilage which is not infiltrated with urates, and by the formation of ecchondroses. Beneath the superficial layer which is incrusted with urates, the cartilage becomes more transparent than usual, and is of a bluish colour; this bluish layer varies in thickness, sometimes it is as thick as the normal cartilaginous covering, at others it is hardly distinguishable. Sometimes the whole cartilage is infiltrated with urates, and the cartilage may even entirely disappear. Histological examination reveals how this bluish line is formed, and by what process the cartilage disappears. In this layer is observed proliferation of the cells with enlargement of the primary capsules: these form lines between which the matrix becomes transparent and splits up. These phenomena of irritation, which are much more marked here than in chronic rheumatism or scrofulous arthritis, cannot, however, lead to the formation of villi, for the inert and infiltrated superficial layer prevents the enlarged capsules opening into the articular cavity. There is frequently, therefore, an accumulation of new cartilage elements resulting in hypertrophy.

Disappearance of the cartilage is brought about by progressive erosion of the superficial infiltrated layers, which, having lost their elasticity, are unable to resist articular friction; the two opposed surfaces hence become eroded by the normal movements of the joint. On treating a section, cut perpendicularly to the surface, with a 40 per cent. solution of potash, this process may be studied. It is then seen that in the superficial layer of cartilage the capsules are round or oval, clearly indicating that the normal superficial layer, formed of flattened capsules, has entirely disappeared. This erosion of cartilage is only seen in very movable joints, the metatarso-phalangeal articulations for example, while in the tarsal articulations, those of the cuneiform bones for instance, it is never seen, even in cases of gout of long standing. When the cartilages have disappeared, a softened chalky mass is left in their place, and separates the two bones, or, as we once had occasion to observe in the metatarso-phalangeal articulation of the big toe, true ankylosis may occur. In place of the articular cavity there were areolæ of cancellous tissue which contained urate of sodium, so that the interarticular line was only represented by a white line. The bones, sawn in two in a longitudinal direction and dried, distinctly showed this singular arrangement. The ankylosis evidently resulted from formative ostitis limited to the extremities of the two bones. These are not the only conditions under which the medullary tissue of bone may be infiltrated with urates; it may be met with, in fact, in extremities of bones in which the investing cartilage has been preserved.

Irritation of the cartilages may, in gouty arthritis, as in other forms of chronic arthritis, induce the formation of ecchondroses. They are developed beneath the synovial membrane, round the margin of the heads of the phalanges, for example; they are generally much smaller than in chronic rheumatism. The periarticular nodosities of gout are principally due to chalk-stones, though they may also be partly produced by ecchondroses.

Gout is never the cause of suppurative arthritis, though in consequence of inflammation, a fluid, having the appearance of pus and containing numerous pus cells, may accumulate in the joint; such a puriform fluid also contains crystals of urate of sodium. Sometimes a very slow form of suppurative and eliminative inflammation is seen near to subcutaneous tophi. The pus then contains, besides pus cells, granules and crystals of urates.

The two periods in the histological lesions of gout are not as marked as the description we have given might lead one to suppose. Deposit of urates may indeed occur in cartilage which is undergoing proliferation ; for primary capsules inclosing a great number of secondary capsules or large spherical capsules, the presence of both of which indicate formative irritation, are often found to contain crystals of urate of sodium. Considering the clinical symptoms, it is very probable that the deposit is continued during the whole duration of the disease. The exacerbations of gout are related to accesses of inflammation in the joints. We know, on the authority of Garrod, that there is no excess of urates in the blood during these exacerbations, while it has been proved, at least in birds in whom the ureters have been tied, that infiltration of urates is dependent on an excess of urates in the blood.

VI. Tumours of the Articulations.

Primary tumours of the tissues which form part of a joint are extremely rare, exception being made for ecchondroses which are formed as the result of arthritis.

Ecchondroses.—The ecchondroses which are found in the intervertebral disks do not seem to be due to inflammation ; we are ignorant of their cause. They are observed at the autopsy of patients who are generally advanced in age, and they are usually multiple. It is known that the intervertebral disks are like diarthrodal cartilages, intimately adherent to the bodies of the vertebræ. On each osseous surface is observed a layer of calcified cartilage, succeeded by a layer of homogeneous or segmented hyaline cartilage which limits a cavity filled with a mucoid substance. The vertebral ecchondroses are developed from the hyaline cartilage. They take the form of two masses held together and separated by a layer of fibro-cartilage which indicates the inter-articular line. In patients advanced in age, these ecchondroses often become ossified, and the osteophytes which result are frequently divided by a horizontal plane, in which fibro-cartilaginous tissue can still be found. This fibro-cartilaginous layer may be invaded by ossification when the two vertebræ become ankylosed.

Arborescent lipoma.—J. Müller has described a variety of lipoma, called arborescent by him, and which is characterised by a series of isolated lobules united in a racemose manner. The synovial fringes normally contain adipose tissue, and arborescent lipoma is simply an exaggeration of this condition. This disease is so rare that we have never met with it.

Tubercle of the synovial membrane. Tubercular arthritis.—Miliary tubercular granulations of the synovial membrane are frequent, though they have only recently been described. In such cases the articular cavity contains pus, the synovial membrane is thickened and transformed into a pulpy membrane, resembling the pyogenic, in which semi-transparent or opaque granulations are observed; on section these granulations are seen to invade the whole thickness of the membrane, they may be discrete or confluent, semi-transparent or caseous (p. 201), and between them is an embryonic tissue, traversed by dilated blood-vessels; the adipose tissue which lines the synovial membrane has disappeared. The cartilage, examined with the naked eye, seems to be normal, or rather it has lost its elasticity, and the surface is no longer smooth. In a case which we examined, there were signs of acute arthritis, the cartilage was superficially softened and split up; the most superficial capsules seemed to have disappeared, and there was cellular proliferation in the deeper capsules. The cancellous tissue of the epiphyses, contrary to what is observed in white swelling, was not rarefied, and the bone corpuscles did not contain fat granules. It is certain that the arthritis which accompanies and follows tuberculous deposit has been hitherto confounded with scrofulous arthritis or white swelling; but it must not hence be concluded that every white swelling is a case of tubercular arthritis. The relative proportion of tubercular arthritis and white swelling cannot be determined on present data.

Tumours developed in adjacent parts and extending into articular cavities.—Tumours of the bones, sarcoma in particular, which is certainly the most frequent variety, rarely penetrate into a joint. The calcified layer of cartilage is not absorbed as readily as bone is under the influence of a neoplasm, and often arrests its progress for a long time. Sometimes, however, this layer gives way, and the morbid mass then penetrates into the joint. This accident is preceded by all the phenomena previously described as those of chronic arthritis by continuity (p. 400).

In the articular cartilages of some subjects, more particularly in children, may be seen holes, looking as if they had been punched out; by means of these communications are established between the joint and a cavity varying in size and which is hollowed in the tissue of an epiphysis. The osseous tissue bordering this cavity is rarefied and filled with granulations infiltrated with pus, or it may be condensed. Inside the cavity, pus or more or less solid caseous matter is found. In such a case the articulation also contains pus, and presents all the morbid appearance of suppurative arthritis. All surgeons, Nélaton in particular, have regarded this lesion as tubercular in origin. Our own histological study of the subject does not enable us to formulate a definite opinion, since we contend that there is nothing specific in caseous degeneration. In the osseous tissue adjoining these losses of substance, we have only found changes due to ostitis, and in the edges of the perforation of the cartilage, proliferation of the cartilage cells as in every other case of chondritis. Before deciding the question, therefore, we must wait for new data based on more recent appearances, or for cases in which, side by side with long-standing alterations, spots may be found presenting the characters of tuberculosis of the bones, such as are observed in Pott's disease; in which disease, side by side with cavities filled with cheesy matter, are found discrete miliary granulations or masses of confluent granulations.

CHAPTER IV.

ALTERATIONS OF CONNECTIVE TISSUE.

I. Congestion and Hæmorrhage of Connective Tissue.

Congestion of connective tissue is often observed during life without leaving traces after death ; when, however, it is connected with inflammation or hæmorrhage, the blood-vessels of the connective tissue are, in the cadaver, often found filled with blood. On removing fragments of this congested tissue with the scissors and examining them in serum, the capillaries are found to be filled with red blood corpuscles, which are crenated twenty-four hours after death. In inflammation the capillaries are dilated in a regular or fusiform manner.

Extravasations of blood into connective tissue are extremely common in contusions, wounds, and diseases accompanied with hæmorrhages. The blood corpuscles escape from the vessels, and are effused between the bundles of connective tissue separating them. In order to study this lesion soon after the hæmorrhage has taken place, the preparation should be hardened in alcohol and sections cut, which, softened in water, stained with carmine, and examined in glycerine rendered slightly acid, show the following appearances: bundles of connective tissue cut across longitudinally or transversely and separated by spaces filled with red blood corpuscles, among which the white corpuscles, solitary or in groups, are easily recognised by the carmine stain which they take. These preparations closely resemble those of cavernous angioma (p. 241).

Ecchymosis.—Later and in a variable space of time, the effused blood undergoes considerable changes; the fibrin which coagulates round the corpuscles and fixes them undergoes molecular metamorphosis; the red blood corpuscles are destroyed, and in their place are found the products of their decomposition, granular hæmatoidin, or at least a red, yellow, or brown substance, one of the derivatives of hæmoglobin, as well as albuminoid granules, and finally fat granules. But at the same time that these metamorphoses of the blood occur, changes of an irritative character are taking place in the connective tissue, the end of which is the elimination of all the products of decomposition. The white corpuscles are seen to be present in large numbers, and when near red blood corpuscles which are still intact, or the coloured granules derived from them, they absorb them, re-enter the circulation of the lymph or blood, and carry away the particles with which they are charged. At the same time the fixed cells of the connective tissue swell and absorb coloured granules. It is to these two histological facts that the complete disappearance of ecchymoses must be attributed, and also the persistent pigmentation of some cicatrices. This description of phenomena following hæmorrhage into cellular tissue is based on observations made on man, and on experiments practised on animals.

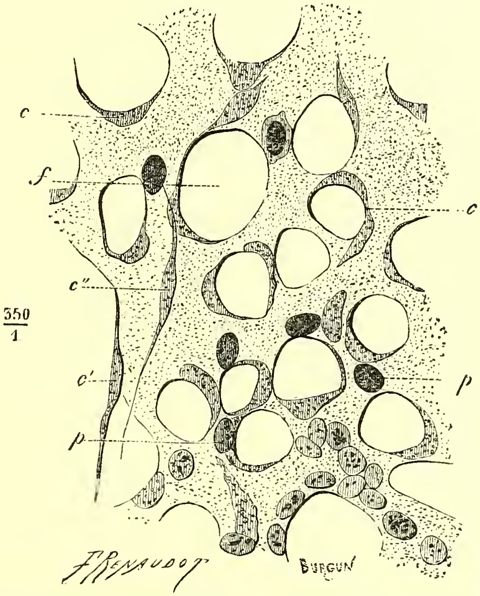

Fig. 220.—Transverse Section of Subcutaneous Connective Tissue from a Wound powdered with Vermilion.

c, connective-tissue cells arranged in the form of a semicircle around the connective-tissue bundles; *f*, connective-tissue bundles rendered transparent by glycerine; *c′* and *c″*, connective-tissue cells seen lengthwise; *p*, lymph cells infiltrated with vermilion, seen in the inter-fascicular spaces, which are enlarged and filled with a granular exudation. The connective-tissue cells represented here are slightly swollen and also contain granules of vermilion.

To these observations others should be added in which the substance effused into the connective tissue was not blood, but a solid and finely pulverised coloured substance always capable of being recognised in the midst of the tissues. Such are powdered vermilion held in suspension in water, and anilin blue precipitated by water from an alcoholic solution. If a cubic centimetre of water, holding one of these substances in suspension, be injected into connective tissue, no free granules will be discovered in the tissue five or six days after the operation. All the granules will be found to have passed either into the lymph cells, or into the tumefied connective-tissue cells, which are more numerous than normally (fig. 220). The lymphatic glands, with which the vessels of the region are in communication, are also found to contain a variable quantity of the coloured granules.

The various tints observed in the skin in ecchymosis are due to the hæmoglobin, which, originally soluble, is changed into coloured granules of hæmatin and hæmatoidin. These granules behave, with regard to the living elements which surround them, in the same way as finely pulverised coloured granules injected into the connective tissue. As described above, they set up an irritation and determine the appearance of a great number of white corpuscles, which absorb and carry them away. Such is the method of absorption in ecchymosis. The irritation produced by coloured granules derived from the blood may be more or less intense; sometimes it passes unperceived, at others it is decidedly suppurative and may give rise to an abscess consequent on extravasation of blood.

II. Œdema.

From the histological point of view, œdema is essentially characterised by an effusion of albuminous serum between the fibres of connective tissue, which it separates from one another. On incising œdematous loose connective tissue, it is found to be transformed into a tremulous, transparent, gelatinous mass, in the midst of which are seen delicate fasciculi, adipose collections, and red lines corresponding to blood-vessels. This appearance results from the serum between the fibres of connective tissue being retained in the same way that water is held in cotton wool. But on isolating a fragment of œdematous connective tissue and leaving it alone, the connective-tissue bundles and the elastic fibres contract, expel the serum, and the tissue returns to its primitive condition. The expulsion of the serum is really due to contraction of the fibres, for on placing the œdematous fragments in serum they still undergo contraction. This property which connective-tissue fibres possess, and which preserves them for a long time in spite of distension, also explains the easy and continuous flow of serum from punctures made in the skin of dropsical patients. The fluid which flows from these punctures is transparent and albuminous; it neither coagulates on contact with the air, nor spontaneously, nor after the addition of red blood corpuscles, which fact indicates that it does not contain fibrinogen. By this fact alone it may be distinguished from the serum of inflammatory fluids. A small number of white blood corpuscles is always found in the serum of œdema.

The histological examination of inflamed connective tissue is easily made: it is enough to remove fragments with curved scissors, place them on a slide, and cover with a cover glass. The manipulation should be rapid so as not to allow the fluid to escape. In such preparations the connective-tissue bundles are seen to be separated from one another, and in the interspaces serum is present containing a larger number of white blood corpuscles or lymph cells than in the normal condition; the cells along the fasciculi, the fixed cells of connective tissue, are seen to be more or less globular, and contain a very distinct nucleus and refractive granules. These granules contain fat, but are not entirely composed of it, for chromic, acetic, and picric acids act upon them in a way which is never seen in granules purely fat; these reagents diminish their diameters while increasing their refractive index. It is probable that they are a combination of fatty principles with an albuminoid substance, which is broken up by the action of the

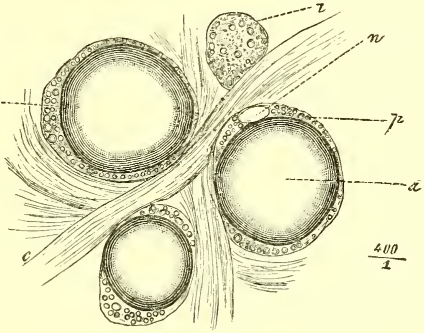

Fig. 221.—Adipose Cells of the Subcutaneous Tissue of the Dog in Artificial Œdema, produced by Ligature of the Inferior Vena Cava and by Section of the Sciatic Nerve.

a, globe of fat; *n*, nucleus of the cell; *p*, protoplasm infiltrated with granules of fat; *r*, connective-tissue cell infiltrated with granules of fat. Magnified 400 diameters.

acids. This is, however, only a hypothesis which we feel ourselves bound to give in the absence of precise chemical data. In the cells of œdematous connective tissue, light yellow granules, very small in size and often angular in shape, are often seen; they are probaly formed from the colouring matter of red blood corpuscles; they are almost constantly met with in the serum of œdema. This pigmentation is particularly observed in long-standing cases of dropsy. The connective-tissue bundles and the elastic fibres undergo no appreciable change. The blood-vessels which traverse the œdematous parts are filled with red blood corpuscles; the proportion of white corpuscles is increased, and they are easily seen along the vascular walls. In some cases the red corpuscles are so numerous and pressed together that they cannot be distinguished, and the blood-vessels appear as if injected by a homogeneous mass. The blood-vessels are easily studied, for they, like the connective-tissue bundles, are isolated by the serum.

The fat cells in œdema generally undergo more or less appreciable changes. In œdema produced artificially in the dog, the protoplasm, which is between the cell wall of the vesicle and the central drop of fat, undergoes granulo-fatty degeneration, from which it results that the entire adipose cell, instead of being formed of a single refractive mass, shows a circle of granules round the central drop of fat. In the œdema of cachexia the fat contained in the cells undergoes partial absorption. This is seen particularly in phthisis. Fragmentation of the fatty mass into minute droplets is also sometimes seen in adipose cells; this phenomenon is due to the presence of an albuminous fluid in the interior of the adipose cells, and is somewhat analogous to the artificial emulsion of fat in albumen. The nuclei of these adipose cells are always distinctly visible. In œdema which develops rapidly, the large connective-tissue cells are infiltrated with a larger quantity of fat granules than in œdema which occurs slowly, as in heart disease for example.

Cause of œdema.—Till recently it was thought that œdema was the result of stasis of the blood. The physiologist Lower explained in a precise manner the method by which dropsy was produced, and his theory was accepted by all pathologists without exception. He thought that when the veins were obliterated and the blood was no longer able to pass from the arteries into the veins, the serum was transuded through the walls of the vessels as through a filter. Hence he explained dropsy by blood stasis. Hodgson, however, on tying a vein in a human subject was unsuccessful in producing œdema. The theory of Lower was then abandoned, when Bouillaud showed that in most cases of localised dropsy obliteration of the corresponding veins was found. Nevertheless it may be observed that clinically dropsy may occur without obliteration of the veins, and that *vice versa* a vein may be obliterated without producing dropsy. In animals, simple ligature of a vein does not produce dropsy, owing to the fact that the collateral circulation is always sufficient to prevent the tension of the blood passing the limit of resistance of the vascular walls; but if, in an animal in which a vein has been tied, the vaso-motor nerves be also divided, a much larger quantity of blood reaches the dilated arteries, and the tension becomes sufficient to cause transudation of the serum. This exaggerated tension is the true cause of dropsy, and all forms of œdema, excepting, perhaps, the œdema of cachexia, may be referred to the same cause. Hence obliteration of the veins is one condition of dropsy, since it augments the blood tension in the corresponding capillaries, and it produces œdema in cases where there is at the same time atony of the vascular system. It suffices to irritate the skin by scratching it with the finger nail for some time to determine a localised œdema, due to paralysis of the blood-vessels. This phenomenon, which is difficult to produce when there has been no previous morbid irritation of the skin, is effected with the greatest facility in a skin affected with urticaria, or in the neighbourhood of stings from insects, pustules of acne, etc., in these cases an œdematous swelling of the skin is seen to rise under the nail. The œdematous swelling which characterises the commencement of phlegmon is related to atony of the vascular walls, and to an increase of blood tension in the vessels. In this way we are able to refer all cases of œdema, whatsoever may be their nature, to the same physiological cause.

III. Inflammation of the Connective Tissue.

When subcutaneous connective tissue is divided by a cutting instrument, inflammation is produced which ends in resolution, and is itself the necessary process by which this end may be attained. From an open wound of the connective tissue blood first escapes; at the end of some hours the surface of the solution of continuity is covered by a thin, opalescent, greyish layer, the plastic lymph of John Hunter. This great anatomist, and many surgeons even to the present day, have maintained that this plastic lymph, which is exuded from the blood-vessels, is susceptible of becoming organised and reproducing the various tissues met with in cicatrices. In this grey layer are found filaments of fibrin, white and red blood corpuscles, and pus cells; beneath this superficial layer it may be observed that the connective-tissue bundles and the capillaries are separated from one another by some coagulated substance, so as to form a kind of continuous and extremely delicate membrane. From this description it is seen that at the moment this so-called plastic lymph takes a solid form, it contains cellular elements. In the present condition of science these facts might be explained by the passage of white corpuscles from the blood-vessels, and of fibrinogen which undergoes coagulation; but this explanation does not probably cover all the ground, for it is possible that the lymph cells contained in the lymphatic vessels and in the meshes of connective tissue may also play an important part in these phenomena. We have indeed already seen that white corpuscles or lymph cells exist in a free state between the fasciculi of connective tissue, and, on the other hand, the conditions of the formation of fibrin are far from being well understood; we only know that the plasma of blood brought into contact with paraglobulin, and a series of other substances contained in histological elements, takes the form of fibrin. The difficult point is to know why blood plasma, lymph, and serum of the pericardium which contain fibrinogen, never give origin to fibrin in the living organism, though these fluids are in contact with elements containing fibrinoplastin.

Suppuration.—The phenomena of superficial exudation, which are originally but slight, soon become exaggerated and take on the characters of suppuration. The connective tissue then becomes more profoundly altered, it loses for the depth of some millimetres its fasciculated appearance, it becomes pulpy, semi-transparent, and embryonic in character. On the second or third day fasciculi of connective tissue are still found in this embryonic layer; they are however swollen, less distinctly fibrillar, and seem to be no longer enveloped by that peculiar layer which limits them and causes them to swell irregularly when acted upon by acetic acid. They are separated from one another by round or angular cells, formed of a mass of protoplasm containing a nucleus. The large flat cells of connective tissue are not generally found in this layer. The infiltration of the connective tissue by an increased number of round cellular elements generally extends to a distance of from two millimetres to one centimetre from the solution of continuity; but this lesion can only be recognised with the microscope. The enlargement of the fixed cells of the connective tissue, the division of their nuclei, and their subsequent proliferation, may be clearly seen in this peripheral zone. Hence we see that the abundant production of new cellular elements between the constituent parts of connective tissue may originte from two sources, from diapedesis of white blood corpuscles, and from multiplication of connective-tissue cells; but in the present condition of science it is impossible to determine the part played by each of these processes in the phenomena of the repair of wounds.

As we have already said, the connective-tissue fasciculi, comprised in the embryonic layer, lose their fibrillar state and become swollen; they are afterwards entirely dissolved, so that not a vestige of them can be found. The granular layer on the surface of wounds or the pyogenic membrane, composed solely of cells and capillaries with embryonic walls, give origin to granulations. The evolution of granulations has already been described when treating of cicatrisation (p. 111).

IV. Purulent Inflammation of Connective Tissue or Acute Phlegmon.

We call acute phlegmon purulent inflammation, for, even when the disease terminates in resolution, there are a great number of pus cells in the meshes of the connective tissue. It is well known with what rapidity acute phlegmon is developed: redness, increase of temperature, œdematous swelling, and acute pain show themselves at once and simultaneously. The opportunity of studying in man the histological changes which occur at the onset in the connective tissue is rarely offered, but the phenomena can be followed in phlegmon produced artificially in animals, and everything leads one to suppose that they are the same in both cases. To produce acute phlegmon in a dog, a few drops of a five per cent. solution of nitrate of silver must be injected into the connective tissue; at the end of from ten to twelve hours there is an œdematous and painful swelling of the region; the connective tissue is gelatiniform, the blood-vessels dilated and filled with blood. At first sight there seems to be no difference between this tissue and that of œdema; but the serum does not flow so easily as in simple œdema, and there are different histological lesions in the two states. In phlegmon, as in œdema, a great number of white blood corpuscles or pus cells may be observed between the connective-tissue bundles, separating them from one another; there is, besides, a fibrinous reticulum which is never seen in simple œdema. We have here indeed acute inflammatory œdema which is very probably related to the same cause as simple œdema, in that it results from paralysis of the blood-vessels and increased blood tension. The capillaries are in fact dilated and filled with blood, from which results an increase of temperature in the affected part. At this period the connective-tissue bundles do not show any appreciable change; the large flat cells swell and tend to take the spherical form, some contain two nuclei and become granular, and even fat granules may be distinguished. This first period of phlegmon is especially characterised by the production of numerous pus cells and a fibrinous exudation; soon the pus cells increase in number, the fibrin becomes more abundant, so that the substance

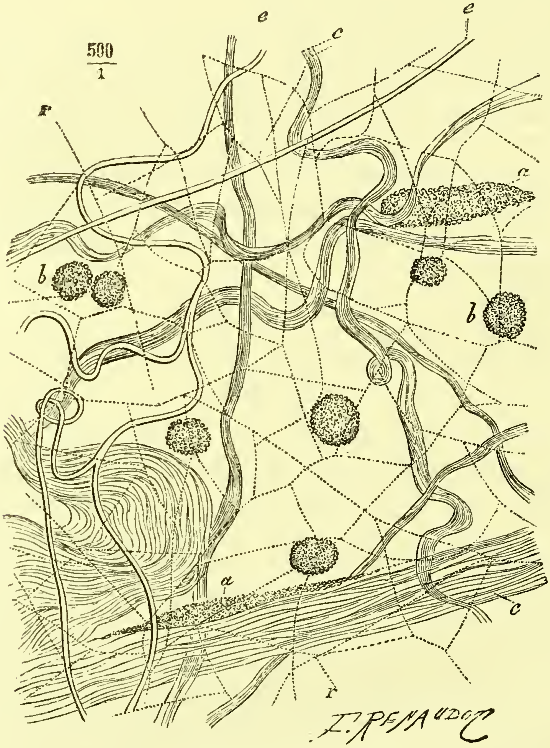

Fig. 222.—Inflammatory Œdema of the Connective Tissue of the Dog, produced by a ·1 per cent. injection of Nitrate of Silver.

The preparation was made by removing a fragment of the œdematous tissue with scissors and slightly pressing it between two slides; at the end of a few hours a fibrinous reticulum was formed, and which is here indicated by the dotted lines *r*; *a*, connective-tissue cells become granular; *b*, pus-cells; *c*, elastic fibres; *e*, connective-tissue bundles. Magnified 500 diameters.

effused between the fibres solidifies, and the inflammatory tumour, becoming firmer, gives on pressure a sensation of resistance to the finger. Fluid which may be displaced as in œdema is, in fact, no longer present. To the presence of fibrin, filling the meshes of the connective tissue, must be attributed the limitation of phlegmon in cases where it develops slowly and in a circumscribed region.

In man to this first period succeeds **resolution, induration,** or **suppuration.** When resolution takes place it is probable that the extravasated white blood corpuscles are taken up by the lymphatics, either in their normal condition or after having undergone molecular dissociation, and that the fibrin and red blood corpuscles disappear in the same way. Induration without suppuration is very similar to induration which takes place after opening an abscess: the histological phenomena are probably the same in both cases. Between the connective-tissue fasciculi fresh cellular elements are formed, and around them may be seen a new transparent ground substance of soft consistence, so that the tissue resembles that of fasciculated sarcoma. Later, these cellular elements undergo fatty degeneration, and all the new tissue is absorbed. All the phases of this process, which are extremely difficult to follow, have not yet been accurately studied. In every case of phlegmon, pus cells are found in the meshes of the connective tissue; but when they are produced in great numbers, and the connective-tissue fasciculi are separated from one another or undergo inflammatory softening or absorption, a purulent collection or abscess is formed, and the phlegmon is said to have suppurated.

Circumscribed phlegmon.—In circumscribed phlegmon the pus is creamy, homogeneous, and does not contain bundles of connective tissue. Examined under the microscope it presents: first, round cells exactly similar to white blood corpuscles and containing only one nucleus; secondly, cells of the same diameter containing many small nuclei; thirdly, similar cells containing a variable number of fat granules; fourthly, large cells measuring 20 μ in diameter and containing fatty granules,—granular bodies; fifthly, entire or broken-up red blood corpuscles. The sac which contains the pus is generally anfractuous, and lined by a layer similar to that which is produced on the surface of a wound on the second day; in this layer, the softened connective tissue fasciculi are united by a layer of coagulated fibrin, inclosing pus cells. When the abscess is opened and emptied, the walls of the emptied sac being brought into contact unite, an induration resulting which lasts a few days. The floor and edges of the abscess secrete pus, in which case the consecutive phenomena are those of a simple wound.

Diffuse phlegmon.—In diffuse phlegmon or diffuse cellulitis, the inflammatory phenomena are so intense that more or less extensive flakes of connective tissue have not time to undergo inflammatory absorption ; they are necrosed *in situ*, and act on the neighbouring parts as foreign bodies. In diffuse cellulitis there is a true necrosis of the connective tissue, and it resembles diffuse phlegmonous ostitis. On opening the purulent foci necrosed flakes of connective tissue are found mixed with pus. On the wall of the abscess are also seen masses of greyish filaments, formed by detached bundles of connective tissue infiltrated with pus. If the patient succumbs at this period, incisions made across the phlegmon show that all the connective tissue of the limb is infiltrated with serum, blood, and pus variously combined. In the midst of the infiltrated parts, opaque whitish masses are observed formed of filaments of mortified connective tissue, more or less free or still adherent, the whole exhaling an odour of gangrene.

On histologically studying this gangrenous connective tissue we find a fibrillar mass in which it is difficult to distinguish fasciculi ; in the midst of the dissociated fibrils are found pus cells, albuminoid granules, yellow or blackish pigment, fat granules, and drops of fat. The latter are probably derived from the destruction of the fat cells. The flakes of connective tissue which are detached and float in the pus show a similar structure. Maceration in the purulent fluid dissolves the cementing substance of the fibrils and sets them free, exactly as if they had been treated by the reagents which are used with this object.

V. Chronic Phlegmon.

The name chronic phlegmon is given to long-continued inflammation of the connective tissue, characterised by lardaceous induration and accompanied most frequently by suppuration. Chronic phlegmon is not a primary disease of the connective tissue, it accompanies chronic affections of the bones or vascular system. The connective tissue is sometimes thickened for a considerable depth, and simulates a tumour, which tumour is, however, never well defined, but blends with the neighbouring sound parts, so that it is difficult to assign to it a limit. On the surface are seen fistulæ, ulcers, or hypertrophied papillæ, regarding which fuller details are given in the article on the pathological anatomy of the skin. On dividing the morbid mass the tissue is seen to have a lardaceous appearance, and a serous or opalescent fluid flows from it. On attentively examining the divided surface there may be seen portions distinctly fibrous which correspond to tendons or aponeuroses ; parts which are semi-transparent and infiltrated with fluid as in œdema ; opaque, purulent, and irregular spots, dilated vessels gorged with blood, and hæmorrhagic points.

In order to examine this complex tissue under the microscope, many methods are used. The elements obtained by dissociation from fresh specimens are pus cells, granular bodies, and cells larger than pus cells and of various forms, globular, fusiform, flat, or irregular, resembling, in fact, those observed in sarcoma. Beside these cellular elements there are fat granules, drops of fat, and connective-tissue fibres. In microscopical sections made after hardening in a ·2 per cent. solution of chromic acid and preserved in glycerine, bundles of connective tissue are found divided in different planes and separated from one another by collections of cells. Some of these cells resemble white blood corpuscles, others, which are larger and fusiform, are fixed connective-tissue cells, more or less modified. The blood-vessels have thickened walls, which have become embryonic in structure, and they are surrounded by an irregular zone of pus cells. Sometimes groups of atrophied adipose cells are found the nuclei of which have multiplied ; they are generally separated from one another by masses of embryonic or pus cells. Finally, here and there, cells similar to those of sarcoma predominate and form collections varying in size.

From this description it is seen that there is no fundamental difference between the structure of this morbid tissue and that of some sarcomata. If two preparations of these different tissues were selected from among those most nearly similar to each other, it would be hardly possible to distinguish one from the other. But on making a complete and comparative analysis of different portions of these neoplasms, characters differentiating the two will be found. Sarcomata, for example, do not contain purulent centres like chronic phlegmon, at least if they are not inflamed. Moreover, in chronic phlegmon the constituent elements of the tissue persist much longer than in a diffuse sarcomatous tumour. Since chronic phlegmon is the result of a cause that can always be determined, such as white swelling, diseased bones, or varicose ulcers, while the cause of the development of sarcoma is unknown, the diagnosis would be always easily made if all the data furnished by the clinical and pathological study of the subject were taken into consideration. Another very important distinguishing character is afforded by therapeutical surgery. When the anatomical cause of chronic phlegmon has been removed, recovery follows; when in a surgical operation, an amputation for example, the flaps contain tissue indurated by chronic phlegmon, a regular cicatrice is still produced, whereas if sarcomatous parts were preserved the tumour would be reproduced with renewed activity.

VI. Tumours of the Connective Tissue.

All tumours, without exception, may be developed in connective tissue, but it must not, therefore, be concluded that the connective-tissue cells are the sole source of these, as Virchow has maintained. We have, in fact, shown that at the commencement of almost all neoplasms constituting tumours, embryonic tissue may be found, and is the point of departure of the new tissue. The method by which embryonic tissue is formed from connective tissue is identical in simple inflammation and at the commencement of a tumour. The cells which compose embryonic tissue are probably white blood corpuscles escaped from the vessels and also connective-tissue cells multiplied by division. We base the opinion that these elements are probably white blood corpuscles on Cohnheim's experiments on the frog; no one has yet attempted to elucidate direct experiments by the development of embryonic tissue in tumours.

The most frequent tumours of loose connective tissue are those which have their analogues in the varieties of this tissue—**fibroma, myxoma, lipoma, sarcoma, carcinoma,** and **syphilitic gummata.** On the other hand, **tubercular granulations** are rare, though it is known that they may be developed on the edges of a wound, the base of an ulcer, and in the inflammatory tissues which surround a fistulous tract, in the walls of scrofulous abscesses, and in certain forms of periostitis (Gaujot and Kiener). Hence the possibility of the primary development of tubercular granulations in loose connective tissue may be conceived, and it is probable that they may be discovered there on looking for them attentively. As to *epithelioma* developed in connective tissue, it always originates in the interpapillary or glandular epithelial tissue, or in embryonic tissue in contact with pre-existing epithelial masses. All the other varieties of tumours, osteomata, chondromata, etc., may be developed in connective tissue.

Serous cysts of the connective tissue are always lined with endothelial cells similar to those of the serous membranes. Their walls are formed by superimposed connective-tissue fibres, between which are flat cells parallel to the surface of the membrane. The development of these cysts has not been studied, but it is probably the same as that of serous bursæ (*vide* p. 296). In subcutaneous connective tissue, hydatid cysts with ecchinococci have been observed. The mother vesicle is surrounded by a complete connective-tissue membrane containing numerous blood-vessels. Hydatid cysts formed by cysticerci have also been met with. A solitary worm occupies the cyst.

CHAPTER V.

LESIONS OF THE SEROUS MEMBRANES.

I. Hæmorrhage of the Serous Membranes.

The lesions of the serous membranes are placed here because they closely resemble those of the connective tissue. We present only a few generalities concerning the lesions of these membranes, as we propose to return to them and describe more minutely the changes of each one, when considering the organs covered by serous membranes.

Hæmorrhage into serous membranes is common ; it is enough to cite meningeal hæmorrhage, circum-uterine hæmatocele, and hæmatocele of the tunica vaginalis. The effused blood coagulates and undergoes the series of metamorphoses always observed in such extravasations, and determines an inflammation of the serous membrane, which inflammation is generally slow, and does not cause suppuration. It produces exudations and new formations in the form of false membranes on the surface, or in the form of adherent bands between the two surfaces of the serous membrane. The retrogressive modifications of the effused blood consist in the disappearance of the red corpuscles, the liberation of the hæmoglobin, the formation of granules of hæmatin, or crystals of hæmatoidin, and the dissociation of the fibrin, etc.

In traumatic hæmorrhage of the serous membranes, notably in hæmorrhage into the peritoneum following a wound of the abdomen, the hæmatin produced by decomposition of the red blood corpuscles is sometimes so abundant that on opening the abdomen it might be thought that soot had been scattered over the great omentum and the intestines. Upon the great omentum a dark substance is seen in the form of opaque, spherical, or angular granules of a very dark brown colour, which are located in the masses of white corpuscles present between the fibres of the reticulum, in the epithelial cells lining these fibres, and in the small cells grouped round adipose cells and which they nearly hide.

In the intestine the peritoneal epithelium is equally infiltrated with black granules, so that it resembles the epithelium of the choroid.

Absorption of the hæmatin granules is probably here affected, as in the connective tissue, by aid of the lymphatic vessels, to which they are conveyed by the white corpuscles. This process may be elucidated by experiment on animals. If into the peritoneal cavity of the rat is injected fresh blood which has been defibrinated and passed through linen, and which has been taken from an animal of the same species, the phenomena observed during the following days are: spherical swelling and proliferation of the epithelial cells of the serous membrane; the penetration of fragmentary or entire red blood corpuscles into the interior of these cells, some of which are detached and float free in the cavity; then the accumulation of lymph cells, which absorb the entire or fragmented red blood corpuscles, and the formation of a fibrinous exudation. The red blood corpuscles undergo modifications, which were first studied by Rindfleisch, and which are similar to those observed on heating the blood to a temperature of 132°; they are decomposed into spherical, refractive, coloured, and perfectly distinct granules, and may be observed in different stages of division.

II. Inflammation of the Serous Membranes.

The essential changes met with in all inflamed serous membranes consist in the formation of exudations, and in the mortification of the epithelial cells. All exudations of inflamed serous membranes contain fibrin, which is not surprising, considering that the fluid of serous cavities normally contains a notable quantity of fibrinogen. The existence of this substance has been ascertained in pericardial fluid, where it always exists in sufficient quantity to be analysed (A. Schmidt). In acute inflammation of the serous membranes this fluid becomes more abundant, and contains a larger quantity of fibrinogen. If, for example, an inflamed pleura be tapped, a limpid fluid is obtained which, when exposed to the air, coagulates in a few hours into a gelatinous mass. Virchow justly remarked that fibrin does not exist already formed in the exudation, but that this simply contains a substance susceptible of producing fibrin when acted upon by the air; hence he called this substance fibrinogen, a name which was adopted by A. Schmidt. It is certain, however, that the action of the air is not the sole cause which determines coagulation of fibrin in this fluid; the addition of red blood corpuscles, or even the serum of blood obtained after coagulation, will give rise to the immediate appearance of fibrin. These changes are very important, for they explain the process of the formation of fibrin, when it is deposited in the form of laminæ on the surface of an inflamed serous membrane, while the distended cavity of the serous membrane simply contains a limpid fluid; this fluid may, however, show fibrinous flakes, or a more or less considerable portion of its mass may undergo coagulation.

When the exuded fluid is abundant and limpid, the exudation is generally called serous, though on the surface of membranes there is always a more or less thick layer of fibrin. This serous fluid nevertheless contains a rather considerable quantity of pus cells held in suspension, and which can only be recognised under the microscope; red blood corpuscles may also be met with. When layers of coagulated fibrin are present on the surface of an inflamed serous membrane, and the fluid contains neither blood nor pus perceptible to the naked eye, the exudation is said to be fibrinous; when the exudation contains blood it is said to be hæmorrhagic, and when it contains a large quantity of pus it is purulent.

Fibrinous inflammation.—The fibrinous exudation formed on the surface of serous membranes varies in its arrangement and appearance. When recent, a reticulum of delicate meshes, with slight depressions between them, is seen on its surface. It is at first thin, but it soon thickens by the deposition of new layers; it is yellowish grey, semi-transparent, gelatinous, soft, and friable. It may be detached with the nail in the form of flakes, which show clean edges when broken. In pericarditis the fibrinous exudation has a peculiar arrangement; its free surface has been compared to the dorsum of the tongue of a cat; it is villous, covered with granulations and laminæ, the arrangement of which is produced by the agitation of the fluid caused by the movements of the heart. When these exudations are old they become smooth, opaque, and are formed of superimposed layers which may be separated by dissection.

In order to study the structure of fibrinous exudations under the microscope, and the modifications of the subjacent serous membrane, recourse may be had to many methods. The simplest consists in removing flakes of the exudation, and examining them after spreading them on a slide. When the exudation is very thin, a beautiful reticulum may be distinguished with a low power; from a thick central point radiate threads of fibres which become thinner as they divide; more delicate threads of fibres unite the latter. When the exudation is thick, or has existed long, this reticulated arrangement cannot be recognised under the microscope. Only on the borders of the specimen may be distinguished torn flakes with sharp edges, or filaments of fibrin. In the midst of these laminæ and fibrils cells may be observed, to examine which recourse must be had to dissociation in a 1 per cent. neutral solution of picro-carminate, or in iodised serum. They vary greatly in form and size; some resemble white blood corpuscles; most of them contain large, distinct, oval nuclei with one or many large brilliant nucleoli, similar to the nuclei formerly considered characteristic of cancer. Some of the cells containing these nuclei are flat, similar to the epithelial cells of serous membranes; others show long processes; some are flat and contain a great number of nuclei (giant cells), and resemble the mother cells of the medulla of bone. Langhans pointed out the existence of these giant cells round the tubercular granulations of serous membranes, but we, as well as Ernest Wagner, have found them in all fibrinous inflammations, as well as in other forms of inflammation of these membranes. To study well the position of these cells in the exudation, and the relations of the exudation with the subjacent membrane as well as the modifications of the latter, vertical sections should be cut, after hardening in alcohol or picric acid—the latter reagent is preferable. The process is as follows: after detaching the serous membrane with the exudation, it should be stretched and fixed with

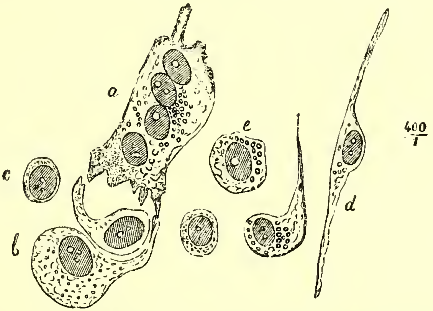

FIG. 223.—ACUTE RHEUMATIC PERICARDITIS; CELLS FROM THE FIBRINOUS EXUDATION OBTAINED BY DISSOCIATION IN A 1 PER CENT. SOLUTION OF PICRO-CARMINATE OF AMMONIA.

a, cell with many nuclei; *b*, racket-shaped cell similar to those found in carcinoma; *c*, *e*, small cells; *d*, flat cell seen sideways. Magnified 400 diameters.

pins on a layer of cork, so that the under-surface of the serous membrane rests on the cork; then the whole is immersed in a concentrated solution of picric acid, of which there must be at least 100 grammes for a specimen of four centimetres square. At the end of two days the process of hardening is complete; delicate sections may then be cut, stained with carmine, and preserved in glycerine. On the surface of the serous membrane a layer of amorphous or granular fibrin is seen, generally bordered by a distinct though sinuous line; beneath are seen the successive layers of cells previously described, and fibrin arranged in a very different manner according to the case. Generally the fibrin forms a network of flattened meshes, which limit elongated alveoli containing cells.

The border of the serous membrane is generally very distinct, the exudation is simply applied to its surface, being here and there separated from it by collections of epithelial cells, forming many layers, and similar to those found in the alveoli of the exudation. It is probable that all these cells proceed from the swollen, proliferating, and detached epithelial cells of the serous membrane. In the present state of science it may be logically maintained that the epithelial cells, modified by inflammation, act like a fibrinoplastic substance and determine the formation of fibrin from the fibrinogen of the originally fluid exudation. The superficial elastic layer of the serous membrane does not seem to be modified in the majority of cases. Between the bundles of the subjacent connective tissue a greater number of cells are observed than normally, which cells resemble white blood corpuscles or lymph cells. Circular, elliptical, or cylindrical, and well-defined spots are also seen, which are the transverse or longitudinal sections of the lymphatic vessels of the serous membrane filled with lymph cells. Ernest Wagner,[1] in a careful analytical study of fibrinous pleurisy, observed that the lymphatic vessels become loaded with fibrin, and concluded that this obstruction of the vessels presented, for some time, a barrier to the absorption of the exudation. We have also found lymphatics filled with fibrin in fibrinous pericarditis and peritonitis, and we have moreover ascertained the existence of modified epithelial cells in the substance of the exudation, and the dilatation of the lymphatics by an accumulation of lymph cells.

Hæmorrhagic inflammation.—Hæmorrhagic inflammation of the serous membranes is characterised by the presence of a more or less considerable quantity of blood added to the fibrinous or fluid exudation. Between simple fibrinous inflammation and true hæmorrhagic inflammation of the serous membranes there are numerous intermediate varieties. In the simplest case ecchymotic spots are scattered over the fibrinous exudation, and may be seen distinctly on its under surface when detached. At other times the fibrinous membrane is red throughout its whole extent, the serous portion of the exudation being also stained with blood. This hæmorrhagic inflammation is most frequently related to the formation of new blood-vessels, which spring up on the surface of the serous membrane and penetrate the under surface of the exudation.

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[1] *Beiträge zur Path. der Pleura* (*Arch. der Heilk.* vol. xi. 1 Heft).

It is very probable that most of the newly formed blood-vessels in the false membrane of serous cavities are developed from vaso-formative cells which enlarge, send out ramifying processes which anastomose and form a complete system already containing blood before communicating with the vascular system. We have not hitherto been able to verify this hypothesis, but the development of blood-vessels in the great omentum on one hand, and on the other the rapidity with which extensive capillary networks are formed in the false membrane of serous cavities, authorise us to admit the hypothesis *à priori*, though unable to verify it by direct observation. The blood-vessels of new formation have embryonic walls, and are surrounded by an embryonic tissue; they form a network in which the principal branches spring in a radiating manner from a central vessel. Thus in hæmorrhagic meningitis (pachymeningitis), small, nummular, red plaques are often found on the internal surface of the dura mater, in which, on examination, fine vascular branches and ecchymotic spots are also discovered. These small plaques, which are the rudiments of extensive new membranes, may be easily detached. The numerous blood-vessels which they contain are filled with blood, and they form a network in connection with the blood-vessels of the dura mater, which fact may be easily recognised on making vertical sections, after hardening with Müller's fluid or with gum and alcohol. When the process is old, false membranes are formed of embryonic tissue and blood-vessels, with layers of fibrin interposed; they are of considerable thickness, and are bathed in a blood-stained exudation.

The blood extravasated into the exudation undergoes a series of modifications, ending finally in the formation of granular or crystalline hæmatoidin. When hæmorrhagic inflammation terminates by suppuration, the fluid contained in the serous cavity contains pus, in which, on careful examination, red granules may be seen with the naked eye. On microscopical examination these red granules are found to be composed of large crystals of hæmatoidin isolated or in groups. These crystals are met with in hæmorrhagic inflammation of the pleura, peritoneum, and tunica vaginalis. It should be added that hæmorrhagic exudations of the serous membranes are particularly observed in alcoholic subjects, and in inflammation resulting from tuberculosis or cancer.

Purulent inflammation.—Purulent inflammation of the serous membranes is primary, or secondary to fibrinous or hæmorrhagic inflammation. Thus, in certain cases of fibrinous pleurisy, in which thoracentesis gives, the first time, a sero-fibrinous fluid, a second puncture, practised many days after the first, may give issue to creamy pus. Inflammation, however, which is purulent from the beginning is much commoner than that which succeeds fibrinous pleurisy; it occurs in puerperal fever, purulent infection, glanders, rheumatism, tuberculosis, etc. In such cases the organs covered by the serous membrane almost always show the different lesions of the disease which has determined the purulent inflammation (metastatic abscess, purulent inflammation, vomicæ, ulcerations, lymphangitis, phlebitis, etc.). When the progress of purulent inflammation is very rapid, the serous cavity is filled with pus, and there is no solid exudation on its surface; the blood-vessels are dilated, their walls embryonic, and the connective tissue of the serous membrane is infiltrated with pus cells located between the vessels. It is almost certain that these pus cells proceed from the blood, and that the epithelium of the serous membrane only takes a small part in their production. In man, the modifications of the epithelium cannot be followed, for at the time that the serous membrane is examined the epithelial lining has disappeared.

In the midst of the pus which fills the serous cavity, yellowish flakes of variable form and size may be met with, composed of a fibrinous reticulum, the meshes of which are filled with pus cells which have generally undergone granulo-fatty change. When the progress of purulent inflammation is less rapid, a fibrinous exudation is formed on the surface of the serous membrane, resembling in structure that of the fibrinous flakes just described. The number of pus cells are so considerable that they may completely mask the fibrinous reticulum, whether the exudation be examined in sections cut after hardening, or without the addition of any reagent. The lymphatics and blood-vessels of the serous membrane show changes similar to those described as present in fibrinous inflammation.

If purulent inflammation follows simple fibrinous inflammation, thick false membranes are found at the autopsy infiltrated with pus, and new vascular formations, similar to those described above as present in hæmorrhagic inflammation; red blood corpuscles or blood pigment derived from them are almost always present.

The pus formed in serous cavities rapidly undergoes nutritive changes; the cells become filled with fat granules, and undergo caseous change if the fluid is partly reabsorbed. This caseous pus forms opaque, yellowish masses of the consistence of mastic; these masses were formerly regarded as tubercular in origin. When the pus remains in a fluid state, the cellular elements are destroyed, or at least in a great part. Crystals of fatty acids and cholesterin are formed, as in caseous foci; most frequently also pigment granules and crystals of hæmatoidin are found. Solid fibrino-purulent exudations undergo similar changes; they become caseous. From their surface are detached flakes which float in the serous cavity; these, as well as the adherent exudation, are formed of a granular substance, the product of the molecular disintegration of fibrin, and elongated collections of fat granules, crystals of fatty acids, cholesterin, and blood pigment.

In old chronic cases of inflammation the serous membrane is considerably thickened and highly vascular, or it may be cartilaginiform. It is then composed of parallel laminæ of connective tissue separated by flat cells; this indurated tissue is exactly similar to that of fibroma with parallel laminæ and flat cells, or lamellar fibroma (*vide* p. 163). This new tissue is very subject to calcareous infiltration, which determines the formation of hard or ossiform plates, more or less regular and extensive. We have never seen true bone corpuscles in these ossiform plates.

Thickening of the pleura is especially seen around masses of caseous pus. Sometimes the alteration is limited to a portion of the serous membrane, which then forms a cyst with thickened walls, containing caseous matter, around which there is, in some rare cases, a transparent gelatinous substance studded with opaque spots. Such an old encysted pleurisy resembles in its entirety an old hydatid cyst. The gelatinous substance which it contains is nothing more than fibrin.

Hyperplastic and adhesive inflammation.—Hyperplastic and adhesive inflammation of the serous membranes is characterised by the formation of connective tissue traversed by blood-vessels, which becomes definitely organised and gives origin to thickenings or adhesions. The latter are seen in the form of bands, or there is a complete fusion of the opposed surfaces of the serous membrane, so that often the pleural cavity is entirely effaced. These adhesions are seen as the consequence of inflammation which shows an adhesive character from the beginning, or they are the result of fibrinous or purulent inflammation; but most frequently it is impossible, when examining old adhesions, to determine their origin. It is even probable that a certain number of them date back to intra-uterine life, and may be due to vices of formation.

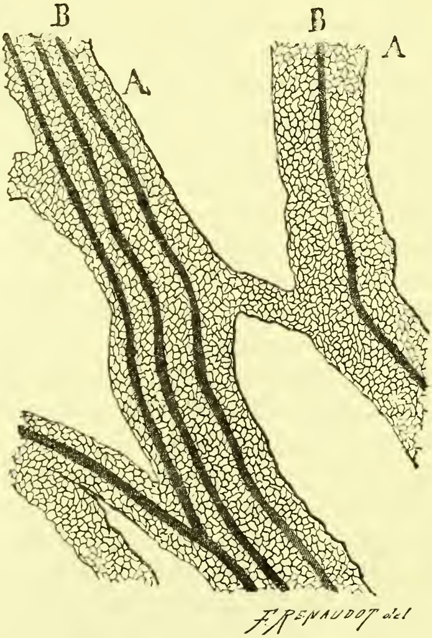

Fig. 224.

A, filamentous bands of the pleura, lined with epithelium; B, blood-vessels. The epithelium is stained with nitrate of silver. Magnified 80 diameters.

In some post-mortems soft vascular growths, composed of embryonic tissue and blood-vessels, may be seen on the surface of serous membranes, particularly on the pleura. These buds increase in size, and if they meet with similar buds springing from the opposite surface, they unite, become fibrous, and form bands varying in form and extent; sometimes they are very thin, sometimes thick, and are always composed of vascular fibrous tissue. Their surface is covered with flat epithelial cells, similar to those lining the rest of the serous cavity. When union is complete, a homogeneous layer of fibrous tissue is found between the two leaves of the serous membrane, uniting them closely together. Thickening of a serous membrane, or hyperplastic inflammation, seems to have the same origin. When only slightly prominent, these thickenings are called milky spots (*plaques laiteuses*), by reason of their whitish appearance, due to the fibrous tissue being composed of superimposed laminæ. When the new growth is thicker, it is composed of cartilaginiform plates, described above. In both the milky and cartilaginiform plates there are a few blood-vessels, or they may be absent altogether. The cartilaginiform plates are sometimes infiltrated with calcareous salts, forming the solid carapaces met with in the pericardium, pleura, peritoneum, and tunica vaginalis. (For further details, see Inflammation of each Serous Cavity.)

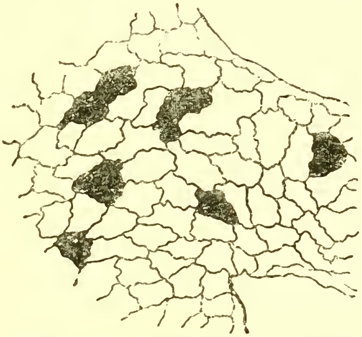

FIG. 225.—EPITHELIUM COVERING THE FILAMENTOUS BANDS WHICH UNITE TWO LAYERS OF THE PLEURA.
Stained with nitrate of silver. Magnified 400 diameters.

III. Tumours of the Serous Membranes.

Primary tumours of the serous membranes are rare, while secondary tumours by propagation or generalisation are common. Primary tumours of the serous membranes are those of which the type is found in the connective tissue: fibroma, lipoma, myxoma, carcinoma, and tubercle.

Fibroma, lipoma, and myxoma.—The most common form of fibroma of the serous membranes is lamellar or corneal fibroma (*vide* p. 163). In many serous cavities villous appendages may be observed, formed of adipose tissue and blood-vessels, and covered by glove-like prolongations of the serous membrane. Such are the appendices epiploicæ of the intestine, the cellulo-adipose folds of the peritoneum, the villosities of the pleura, and the synovial fringes of the articulations. These cellulo-adipose appendages are subject to hypertrophy and form arborescent lipomata, which are slow in their evolution ; they are only discovered after death. In these same appendages mucous or fibrous tissue may be formed, constituting pedunculated myxomata or fibromata.

Tubercle.—Miliary tubercular eruptions of the serous membranes are common. They may be primary or related to general miliary tuberculosis, or they may be developed in the neighbourhood of tubercular foci of organs covered by serous membranes. These granulations are prominent, lenticular, whitish, semi-transparent, non-vascular, sometimes opaque at their centre. The smallest are hardly visible to the naked eye. When numerous they unite and form more or less extensive masses with festooned borders and uneven surface. The largest may attain the size of a lentil. In their neighbourhood the serous membrane is congested, and ecchymotic spots may even be observed. These spots are frequent in the peritoneum, where tubercular granulations may often be seen surrounded by red, violet, slate-coloured, or blackish ecchymoses. These granulations are more common on the visceral layer of serous membranes, though it is not rare to see a larger number on the parietal than on the visceral layer.

Tubercular granulations of the serous membranes are very superficial, appearing sometimes as if they were superimposed on the membrane. They are often seated in the substance of the various layers of the serous membrane, which then acquires a considerable thickness, and presents the signs of interstitial inflammation. Thus in the peritoneum, particularly in the great omentum, the united layers and destroyed trabeculæ may be replaced by a solid mass, one or two centimetres in thickness, formed of tubercular granulations, imbedded in a soft and vascular tissue. This alteration is sometimes mistaken for cancer.

The development of tubercle determines various forms of inflammation in serous membranes, fibrinous, hæmorrhagic, purulent, or formative inflammation. Most frequently, when the tubercular eruption is recent, the whole surface of the serous membrane is covered with a thin and transparent fibrinous layer, which is easily detached, some granulations being often removed with it. Beneath this false membrane the serous membrane does not seem to have suffered any loss of substance. In other cases the fibrinous exudation is so profuse that at first sight the tubercular granulations which are beneath are not perceived: this is generally the case when the exuded fluid is hæmorrhagic or purulent, but on detaching the exudation and washing the surface of the serous membrane the granulations are perceived.

Chronic tubercular inflammation nearly always gives origin to soft vascular buds, of variable extent, covered with exudation; and in their tissue new tubercular granulations are developed. These buds undergo caseous degeneration, in which case the connective tissue of the serous membrane is seen to be thickened, softened, and transformed into embryonic tissue, in which numerous tubercular granulations are developed. Under the influence of the inflammation which accompanies tubercle filamentous buds or bands, which are also often invaded by granulations, are formed between the opposing surfaces of the serous membrane.

The tubercular granulations of serous membranes are at their commencement formed of small cellular elements pressed together, and which blend insensibly with the cells of the superficial or the deep layers of the membrane. These peripheral cells are similar to those which have been described above in fibrinous exudation. They are round or flat, some are many hundredths of a millimetre in diameter, and are filled with nuclei—mother cells or giant cells. They have been described in tubercular pleurisy by Langhans.

When the tubercular eruption is profuse the connective tissue of the serous membrane is modified, and between its fasciculi a variable quantity of embryonic cells are found. The blood-vessels are dilated, and the lymphatics are filled with lymph cells.

The exudation which accompanies tubercular granulations presents the characters studied already when considering forms of inflammation (*vide* p. 100).

As to the thickenings and buds developed on the surface of serous membranes, they are composed of embryonic tissue containing capillaries, the walls of which are formed of tumefied cells. When there is an evolution of tubercles in these buds, the blood-vessels present the modifications which have been described on page 202.

Tubercular granulations on the surface of serous membranes are certainly not always developed from the connective tissue of these membranes, for beneath the tubercles cells are found which seem to be derived from the epithelial layer, and,

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further, the layer of connective and elastic tissue which forms the corium of the serous membrane has not at these points suffered any loss of substance; the question is therefore if the cellular elements of tubercle are derived from the epithelium of the serous membrane, or from the white blood corpuscles, or from these two sources simultaneously. In the present state of science it is difficult to answer this question decisively. Rindfleisch maintained, at the time when diapedesis of white blood corpuscles was unknown, that proliferating epithelial cells were the origin of tubercle: it is very probable that these cells take some part in the formation of superficial granulations, but it has not been shown that they are their sole source. M. Martin is of opinion, after examining tubercles of the peritoneum produced by inoculation in the rabbit, that they are developed under the epithelium from migratory cells derived from the blood-vessels. When tubercular granulations are developed in the substance of the connective tissue of serous membranes,[1] or in the buds of inflammatory tissue, we think that they are developed from an embryonic tissue, which is derived either from the proliferating fixed cells of the connective tissue, or from the white corpuscles of the blood.

Carcinoma.—Primary carcinoma of the serous membrane is rare, but secondary carcinoma by extension or generalisation is, on the contrary, very frequent. Of all forms of primary carcinoma the most frequently observed is colloid carcinoma of the peritoneum, situated either on the peritoneal surface of the liver, or stomach, or in the great omentum. It takes the form of gelatinous plates, with vascular markings and ecchymotic spots. It is developed in the corium of the serous membrane, or in the sub-serous connective tissue. In the great omentum, the reticulated layers are transformed into a matted mass, in which nothing is found recalling the structure of the omentum, but simply that of colloid carcinoma. Other species of carcinoma are developed in the organs covered by serous membrane, and they increase till they form round or budding masses; they produce an inflammation in the membrane the exudation of which is almost always hæmorrhagic.

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[1] According to MM. Keiner and Poulet (*Comptes rendus de l'Académie des Sciences*, January 26, 1880), tubercle of the serous membranes is in its simplest form produced by a spherical or fusiform swelling of a blood-vessel, more rarely of a lymphatic vessel, and by the accumulation around this swelling of a certain number of cells. In the case of a true capillary vessel, the vascular swelling is caused by hypertrophy and hyperplasia of the endothelial cells of a limited portion of the vessel. These cells undergo vitreous degeneration and become fused into a solid cylinder, which on transverse section has the appearance of a giant cell with a marginal circle of nuclei. A tubercle of the peritoneum visible to the naked eye has, according to M. Keiner, the appearance of a milky spot on this membrane in young rabbits (*vide* p. 110).

When a carcinomatous mass is formed upon a serous membrane, secondary smaller masses, which are disconnected, nummular, and have an umbilical central depression, are generally developed around it. The depression is caused by the granulo-fatty degeneration of the centre, and particularly by the more active development of the periphery of the nodule. The lymphatic vessels which pass from these morbid masses often form on the serous membrane hard, knotty, whitish cords, isolated or arranged in a network, and small carcinomatous secondary nodules are developed in their track. The tissue of the serous membrane round these degenerated lymphatics and secondary nodules is always highly vascular; the blood-vessels are dilated and have embryonic walls.

Cylindrical-celled epithelioma may be propagated to the serous membranes, but it is rare; more frequently an epithelioma of this kind, when developed in the intestine, stomach, or bile ducts, determines secondary growths, often of considerable size, in the liver without the serous membrane being affected, while the contrary is generally the case in carcinoma.

Sarcoma, pavement epithelioma, and **chondroma** are very rare, and are never found except as secondary growths. **Osteoid tumours** are often propagated to serous membranes.

CHAPTER VI.

THE ALTERATIONS OF MUSCULAR TISSUE.

I. Normal Histology of the Striated Muscles of Animla Life.

THERE are three species of muscular tissue: first, the striated muscles of the trunk and limbs; second, the cardiac muscle; and third, the smooth muscles. Smooth muscle fibres enter into the composition of blood-vessels; hence we may consider the anatomical lesions of blood-vessels immediately after describing the pathological anatomy of unstriped muscular tissue. The muscle fibres of the heart, by reason of their peculiar structure, have lesions which differ in certain points from those of the striated muscles of the limbs. These lesions will be described in the chapter which treats of the pathological modifications of the endocardium and pericardium. Consequently, with muscular tissue, and following it, we shall study, first, the pathological changes of the blood; second, morbid changes in the heart; third, changes in the blood-vessels; fourth, lesions of the lymphatic system.

The striped voluntary muscles are essentially characterised by striated muscular fasciculi, described on page 28. These fasciculi are arranged parallel to one another, and they are united by extremely delicate fibres of connective tissue, so as to form distinct groups known as secondary fasciculi. These are not surrounded by a continuous amorphous membrane such as the sarcolemma which limits the primitive fasciculi.[1] The arteries and veins ramify between the secondary fasciculi, into which the capillaries penetrate, to insinuate themselves between the primitive bundles, round which they form a network with oblong meshes. These vessels are always outside the sarcolemma.

The entire muscle is enclosed in an aponeurosis, formed of closely united bundles of connective tissue; these bundles are, however, capable of separation, for on injecting a fluid into the muscle under the aponeurosis it will penetrate this fibrous covering, and be found on the external surface of the muscle. By the same process, also, it may be seen that fluid can penetrate throughout the whole thickness of the muscle, between the primitive bundles, the connective-tissue fibres, and the blood-vessels; from which the conclusion is drawn that a muscle possesses a vast lacunar interstitial system belonging to the connective tissue, and in communication with the lymphatic system. Muscles are inserted by means of tendons. For a long time it was thought that the primitive fasciculi of the muscles were directly continuous with the fibres of the tendon. Kölliker, however, had already ascertained that when muscular fasciculi are inserted obliquely on to a tendinous surface, there is no continuity; but he still thought that, in the case in which the tendinous fibres have the same direction as the muscular fibres, they were continuous. Since Weismann used the chemical method of dissociating by a 40 per cent. solution of potash, the insertion of muscular fasciculi into tendons has been understood; the union is accomplished by means of an organic cement of uniting substance, which, acted upon by the potash, softens, and is finally completely dissolved.

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[1] In England the term muscular fibre is generally used for that here translated primitive fasciculus (*faisceau primitif*); but I have thought it well to adhere to the terms primitive and secondary fasciculus, used in the original, as they are evidently preferred by MM. Cornil and Ranvier.—TR.

The termination of nerves in muscles is, from the physiological point of view, a subject of great interest, but hitherto no lesions of the special organs of the nerve ends called the motor plates have been discovered, hence we shall not consider this subject.

In lesions of the muscles we have to study those which relate to the primitive fasciculi on the one side, and to the connective tissue on the other. The lesions of the connective tissue of muscles are those of this tissue generally considered, but the elementary lesions of the primitive fasciculi necessitate a special description, which we shall give before studying the pathological lesions of muscles considered as organs.

II. Lesions of Nutrition of the Primitive Muscular Fasciculi, and of the Muscles themselves.

The lesions of the primitive muscular fasciculi consist in changes of nutrition of their striated substance or multiplication of their nuclei; frequently, however, lesions of nutrition are accompanied with division of the nuclei, but these two phenomena are not always associated, and there are cases in which, without any nutritive modification of the striated substance, multiplication of the muscular nuclei are observed: on the other hand, very advanced lesions of the contractile substance may occur without any alteration of the nuclei.

Atrophy of the muscular fasciculi.—Atrophy of the muscular fasciculi may be coincident with general atrophy of the muscle; or, on the contrary, with the preservation and even with increase in size of the whole muscle, when it is the connective tissue or interstitial adipose tissue which increases. The different tumours of the muscles also constantly cause atrophy of the muscular fasciculi. In emaciation, the muscular fasciculi of the whole body are atrophied, and in infantile paralysis all the fasciculi of a single muscle may be affected simultaneously, or, as in the case of serious febrile disease, only a few may be affected. It is a doubtful point if in man the muscular fasciculi are normally renewed, for in an adult very considerable variations of diameter may be observed in the different fasciculi of the same muscle: some are hardly ·01 mm. in diameter, while others are from ·03 to ·07 mm., or even more. In persons advancing in age this difference is still more marked, and in their muscles fasciculi are constantly found in an atrophied condition, and containing fat granules.

Atrophy is simple or caused by some one of the nutritive changes considered later. These changes generally cause an increase in the size of the fasciculi at the beginning, the atrophy only occurring later. Atrophied muscular fasciculi are of the most varied forms and sizes. If in an adult the fasciculi do not exceed ·04 mm. in diameter, it may be concluded that there is muscular atrophy; when all the fasciculi have a mean diameter of ·01 mm., the atrophy is considerable. Finally the muscular substance may be found to have completely disappeared, at least some of the fasciculi are only represented by rectilinear filaments, formed of collapsed sarcolemma. It is concluded that these are the sarcolemmic sheaths, for between them and recognisable muscular fasciculi all intermediate forms may be found. In some cases in which the muscular atrophy is very considerable and regular, the characteristic striation may be manifestly preserved in fasciculi having only a diameter of ·003 mm. These fasciculi contain nuclei, at which slight swellings are seen. This form may be observed in progressive muscular atrophy, in the last period of infantile muscular paralysis, and in all forms of atrophy dependent on the nervous system.

In some cases of club-foot and infantile paralysis there is an increase of the connective tissue which counterbalances the atrophy of the muscular fasciculi, so that, though the muscle is really atrophied in its active elements, it is considerably larger than normally. This increase in size is particularly shown when adipose tissue is deposited in large quantities between the atrophied muscular fasciculi; this is what occurs in the disease called by Duchenne *pseudo-hypertrophic paralysis.* The atrophied muscular fasciculi, which are few in number, preserve their normal structure, and show neither fat granules nor anything abnormal, excepting decrease in diameter. These thin fasciculi are to a certain extent lost in a mass of very abundant cellulo-adipose tissue, which is substituted for the atrophied fasciculi. This lesion of the muscles is the only one which can be found in the post-mortem examination

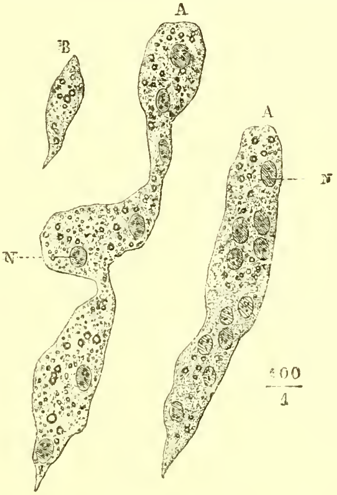

Fig. 226.—Atrophied Muscular Fasciculi undergoing Fatty Degeneration. From a Myxoma.

a, primitive fasciculi in which nuclei, *n*, are seen ; *b*, atrophied and fusiform fasciculus.

of patients who have succumbed to this disease ; the nerves of the medulla were normal in the cases reported by various authors, more particularly by Cohnheim, Charcot, and Joffroy, and more recently by one of us in a case of M. Bergeron's.

In tumours of the muscles the pathological growths develop in irregular spots ; the muscular fibres undergo in places complete atrophy, while throughout the rest of their extent they may preserve their original size ; from which it results that the fibres are divided into irregular segments, the extremities of which are round or drawn out into a point ; generally in the preserved portions, numerous nuclei are disseminated in a granular substance, which replaces the striated substance. These spots resemble cells with multiple nuclei (fig. 210).

Muscular hypertrophy.—This subject has been hitherto little studied. The histological analysis of muscular hypertrophy is very difficult, and raises problems which are far from being solved. When a muscle increases in size from exercise, in a perfectly normal manner, as for example in consequence of gymnastics, or pathologically, as occurs in the intercostal muscles in emphysema, it is very difficult to say if the hypertrophy is due to the formation of new muscular fasciculi, or to the enlargement of old fasciculi. The difficulty is caused by the fact that the fasciculi normally have very different diameters in the same muscle. A fasciculus of ·03 mm. may, for example, attain a diameter of ·05 or ·06 mm. in the course of the process, without our knowing if this size is accidental.

When hypertrophy of a muscle is due to the formation of new muscle elements, the process of this new formation may be followed. Thus Bardeleben studied the genesis of new muscular fasciculi from connective-tissue cells, in hypertrophied intercostal muscles from prolonged dyspnœa. The reproduction of muscular fasciculi in the adult takes place, moreover, in a constant manner, when in consequence of an acute disease a certain number of muscular fasciculi have been destroyed, by one of the nutritive changes to be studied further on. The physiological reconstruction of the muscles, after febrile emaciation, is due, not only to an increase in the size of the atrophied muscular fasciculi, which have preserved their structure, but also to the formation *de novo* of muscular fasciculi, which originate and are developed between the old elements. These phenomena have been well studied by Zenker in various febrile affections—typhoid fever, variola, scarlet fever, etc.—in which he has described the changes and reproduction of muscular fasciculi. The same year that Zenker made these researches, Colberg discovered a similar regeneration of muscles after trichinosis. New muscular fibres are always developed from cells situated outside the fasciculi; the nuclei of these cells multiply, their protoplasm increases and sends out blunt or pointed processes presenting a striking resemblance to the mother cells of bone medulla. The extremities of adjacent cells unite, their substance becomes segmented transversely, and takes the characters of striated muscular substance. But it is improbable that this is what takes place; we know, in fact, that striated muscular fasciculi are not formed from cells placed end to end and united together, but that each fasciculus is developed from a single cell, the nuclei of which multiply.

Hypertrophy of a muscle is not always related to increase of size of its fasciculi, nor to their new formation; it may be due, as we have already said, to increase of connective or adipose tissue, or even to the abnormal development of blood capillaries or lymphatics. We have already spoken of pseudo-hypertrophic paralysis of the muscles: it must also be added that congenital hypertrophy of the tongue is principally due to considerable thickening of the connective tissue of this organ, or to dilatation of the lymphatics.

Granular change of the muscular fasciculi.—This change corresponds to what Virchow has called cloudy tumefaction. It is very often the first stage in fatty degeneration. In this lesion the muscular fasciculi are more opaque than usual, their substance shows numerous fine granules, their striation is indistinct or has even entirely disappeared. When acted upon by acetic acid these fine granules disappear, the fasciculi become transparent, and the striation is less distinct than when normal fasciculi are treated by the same reagent: the striation may even disappear. In other cases, acetic acid, in causing the disappearance of these fine granules, discovers other transparent and refractive granules of a fatty nature, existing in small or large numbers. The sarcolemma is as transparent as usual, the subjacent nuclei are normal, or show signs of proliferation. Whenever this granular state of the muscles is accompanied with proliferation of the nuclei of the sarcolemma, parenchymatous inflammation is present; in fact, this lesion may be observed in inflammation of the muscles, for example, in suppurating intermuscular phlegmon; but it is also met with in cases where the inflammatory nature is doubtful, for example, in all serious acute general diseases—typhoid fever, eruptive fevers, purulent infection, and acute phthisis, etc. In an acute fever this granular change is most frequently accompanied with fatty and vitreous change. When the existence of this change is suspected, the greatest care must be taken in the preparation of the muscles, and we will here indicate the method which should be employed in studying all the alterations about to be considered.

An incision being first made in a muscle parallel to the direction of its fasciculi, a small flake of the muscular tissue is removed by four incisions made with a very sharp razor; this is placed on a slide, and slightly moistened; then with needles, placed at one of the extremities of the divided fasciculi, the specimen is divided in two; the needles are again used in the same way at the same extremity, and the secondary fasciculus is again divided. This method of division is continued till the primitive fasciculi are isolated, or delicate bundles of these fasciculi. The ends of these, which have been touched by the needles, may be disregarded in the examination, for they show an alteration of their contractile substance which might be mistaken for granular change.

Fatty degeneration of muscles.—In a child, as well as in an adult, a few muscular fasciculi may always be found, containing extremely fine fat granules which are rendered visible by the action of acetic acid. These granules are few in number, and attentive care is necessary for their recognition. In old age, the number of granulo-fatty fasciculi is larger; the fasciculi, moreover, contain larger fat granules, which may be easily seen without having recourse to acetic acid. A certain quantity of fat is always present in muscles, but it is in a state of soluble combination, that is to say, it exists as a soap, and is hence not visible under the microscope. When isolated, fat is seen in the form of an insoluble substance. Microscopical analysis does not, therfore, give any idea of the quantity of fat contained in a muscle, but only of that which is in the state of neutral or insoluble fat; hence it results that chemical analysis of a muscle, in a moderate condition of fatty degeneration, does not yield more fat than a normal muscle (Rindfleisch). Nevertheless, the presence of a great number of fat granules in the primitive fasciculi always indicates an important nutritive trouble, for fat in this condition cannot be utilised by the muscles during work like the fat of composition, and it even hinders the play of those organs.

Muscular fasciculi, which have undergone fatty degeneration, are more friable than normal, hence more care must be used in preparing them for microscopical examination. The fat granules of the degenerated fasciculi have a certain regular arrangement; they are deposited in series in the longitudinal striæ of the primitive fasciculi; their presence even marks the longitudinal striation of these fasciculi, while the transverse striation is less distinct, or may even have disappeared. These details may be seen on examining fatty degenerated muscular fasciculi with a power magnifying 250 diameters; with a lower power, only the granular state and the opacity of the fasciculi can be perceived. The sarcolemma preserves its transparency, as may be easily observed at the points where the muscular substance is torn and contracted; the nuclei are also preserved, the protoplasm surrounding them is fatty, and it is in the neighbourhood of these nuclei and the surrounding protoplasm that the process of degeneration commences.

It is very probable that fasciculi having undergone fatty change may return to their normal condition, if what takes place in frogs may be considered as typical. In these animals during the winter a great number of fasciculi become fatty which in the snmmer return to their normal condition. But in man the fasciculi which have undergone this change in disease are most frequently destroyed by a process the different phases of which may be followed. The granules of fat become more and more profuse, the fasciculi become opaque, striation is no longer distinguished, and at the end of the process the sarcolemmic sheath is filled with a formless mass containing a large number of fat granules; these slowly disappear, until finally only the collapsed sarcolemma is left. It is principally in tumours of the muscles, and in callus when it has encroached upon muscular tissue, that the details of these changes may be followed.

In infantile paralysis and in progressive muscular atrophy the muscular fasciculi totally or partly disappear in consequence of fatty degeneration. Fatty change of the muscles is also met with in fevers and in purulent infection; it is very marked in metastatic inflammation of the muscles, while in the case of white infarcts consequent on arterial obliteration by an embolus, the muscular fasciculi are not found to undergo fatty degeneration. In wounds implicating the muscles a few fibres may sometimes be found in a state of fatty degeneration in the embryonic tissue at the base of the wound, but at a little distance, though there is a marked increase of new cells between the muscular fibres, the fasciculi are degenerated. In poisoning from phosphorus, arsenic, etc., fatty degeneration of the muscles is very marked.

Pigmentary degeneration.—In the cardiac muscle physiologically, but only pathologically in other muscles, may be found round or angular granules of a more or less dark-brown colour, located under the sarcolemma, or in the muscular substance itself. These pigment granules are very probably derived from the transformation of the colouring matter of the muscles, which is similar to that of the blood, and has been named muscular hæmoglobin.

This change of the muscular hæmoglobin into pigment is produced when the muscle dies in the midst of a living organism (the heart being always excepted), for example in infarcts and in metastatic abscesses. The fœtus which has remained for some weeks in the uterine cavity after death also shows pigment granules in the muscles.

Vitreous degeneration.—We have already spoken of this form of degeneration on page 68, and we have given it the name of vitreous degeneration, which seems to us preferable to that of waxy change, given by Zenker, who was the first to describe this lesion. This alteration of the muscles must not be mistaken for a modification of the muscular fibre, produced by the method of preparation. On removing a fragment of muscular tissue from the living animal, or from one just killed, the fasciculi contract and form refractive masses, in which striation cannot be distinguished, or only an extremely fine striation, which may be recognised with a high power on shading the field of the microscope. On extending the tongue of a frog with pins, as is usually done to study the circulation of the blood in this organ, it often happens that as a result of the tension the muscular fibres are ruptured and form refractive masses; but after studying the true characters of the lesion,

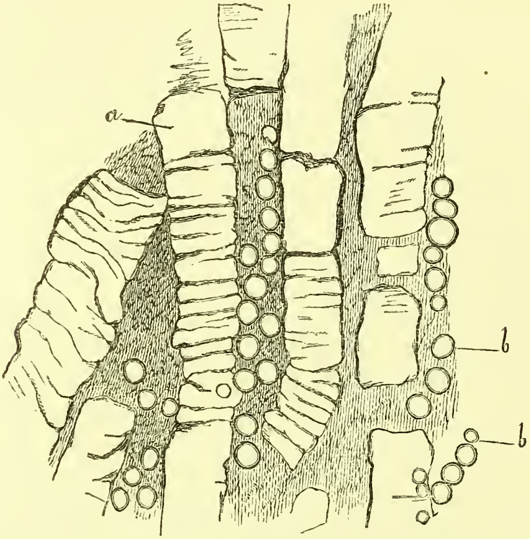

Fig. 227.—Muscular Fibres in a State of Vitreous Degeneration.
a, altered fasciculi; *b*, adipose cells. Magnified 300 diameters.

vitreous degeneration cannot be mistaken for these altogether accidental changes.

Vitreous degeneration consists in a change of the muscular substance, by which it loses its striation, becomes hyaline, and transparent as glass. In this first stage the mucular fasciculi are increased in size, and have preserved their regular cylindrical form, their nuclei are more visible than normally, and the sarcolemma seems to have undergone no modification—indeed the nuclei and the protoplasm which surrounds them have entirely escaped the vitreous change. The vitreous substance stains deeply with neutral carmine; acetic acid causes it to swell without dissolving it. It is much more brittle than muscular substance, so that if not dissociated with the greatest care numerous and irregular fractures are produced. When by means of this process a small cylinder of the muscular fasciculus has been isolated, it becomes separated from the rest of the fasciculus. Thus in the same fasciculus may be seen a series of fragments, separated by spaces varying in size, at which the collapsed sarcolemma seems to be strangulated. The collapsed sarcolemma, compressing the broken extremities of these fragments, gives them the appearance of a number of superimposed casks.

Vitreous degeneration is always limited; it is never met with in all the fasciculi of a muscle, so that if, instead of examining an isolated primitive fasciculus, a group of fasciculi be examined with a low power, some among them are seen to have become homogeneous and transparent. Along their edges is seen a characteristic brightness, due to the refrangibility of their substance; the other fasciculi are intact, or only show granular change. Vitreous fasciculi have lost their physiological properties; those which are intact are, however, still capable of contraction, and they act mechanically on the brittle and inert fasciculi, and by their movements determine the ultimate changes in the vitreous fibres. These changes are particularly well marked in chronic vitreous degeneration, such as may be observed in the neighbourhood of tumours, or better still in chronic phlegmon, around fistulous tracts in caries, necrosis, or white swelling. Vitreous degeneration in such situations has been hitherto ill described, for it has been particularly sought for in acute diseases, such as typhoid fever. In chronic degeneration of the fibres it is impossible to assert if the peculiar appearance of the fasciculi is due to the method of preparation. Under the influence of the movements of the healthy muscular fibres the vitreous substance becomes fragmented in every direction, and is separated into blocks, the arrangement of which often resembles that of bricks in a wall (*vide* fig. 228). Towards the end of the process the fragments become smaller and smaller and form granules, each one of which preserves the optical characters of vitreous substance. It is then that absorption commences, the sarcolemma collapses, and the subjacent nuclei become larger and more numerous, many of them showing signs of multiplication by division; this proliferation of the nuclei seems to be a phenomenon consecutive to degeneration.

In acute fevers, when a certain number of the muscular fasciculi have been destroyed, a new formation of muscular fibres may be observed by which the muscles are completely regenerated. This regeneration has been followed by Zenker, who gives a minute description of it. The cells of the connective tissue adjoining the diseased fasciculi increase in size, their nuclei multiply without division of their protoplasm, they then elongate in the direction of the fasciculi, and before they lose the character of cells to take that of primitive fasciculi they already show a manifest striation. There is here a development which does not essentially differ from the physiological development of striated muscle.

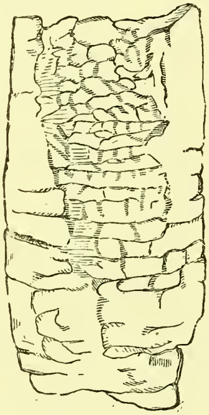

Fig. 228.—Advanced Vitreous Degeneration of Long Standing in a Muscular Fasciculus.
Magnified 350 diameters.

The muscles affected by vitreous degeneration are brittle and easily ruptured: this accident is particularly seen in muscles still capable of use, such as, for example, the rectus abdominis in bedridden persons. The changes which take place in a rupture of the muscle, consequent on this degeneration, will be studied later when considering hæmorrhage of the muscles.

The cause of vitreous degeneration is local or general; in the first case the lesion is limited to the seat of the affection which has caused it, as may be seen in the neighbourhood of tumours, abscesses, and chronic phlegmon. When the disease occurs in consequence of a fever, it is seen particularly in the internal muscles of the thigh and in the rectus abdominis, though it may also be found in other regions. It is very difficult or even impossible to recognise vitreous degeneration with the naked eye. Zenker, however, indicates a peculiar colour similar to that of the flesh of fish, but this colour may be found in muscles which do not show this degeneration, so that histological examination is necessary for its determination.

Hæmorrhage into muscles.—Simple congestion of muscles is not shown by evident signs in the cadaver, except in the neighbourhood of inflammatory or hæmorrhagic foci. Hæmorrhage into muscles was called by the old French and German authors by the name of hæmorrhagic infarctus, but this name does not imply the idea of a primary vascular obliteration. Hæmorrhage into muscles may be caused by contusions, wounds, rupture of a muscle, or may depend on a general hæmorrhagic disease, such as purpura, scurvy, exanthematous fevers, leucocythæmia, etc. When muscular hæmorrhage is recent, it forms in the substance of the muscle a dark red mass, divided sharply from the bright red of the muscular tissue. This mass, of very variable form and extent, may be limited or diffused. As the blood coagulates, the muscle at this point becomes firmer and loses its elasticity. The muscular fasciculi contained in these foci undergo no change or are simply granular.

In order to study the relation of the blood with the muscular fasciculi and the blood-vessels, the specimens should be hardened in alcohol, and delicate transverse sections cut, stained with carmine, and examined in glycerine: the muscular fasciculi are then seen to be separated from one another by masses of red blood corpuscles; in these masses, and between the fasciculi, the capillaries and vessels of a larger calibre are dilated and filled with blood corpuscles. The blood is seen to be coagulated in the vessels, as well as in the inter-fascicular spaces, in consequence of the arrest of the circulation.

When hæmorrhage results from rupture of a muscle, the fragments of the torn muscle are separated, and the space between them is filled with blood, which is at first liquid and then undergoes coagulation; the torn fasciculi project into the focus, the blood infiltrating between them for a greater or less distance. The muscular fasciculi then undergo alterations, which differ according to the cause of the rupture: sometimes it is vitreous degeneration, sometimes granulo-fatty change, but at the point where the fibres are torn they are in a state of complete fatty degeneration; this is particularly observed in the recti muscles of the abdomen when ruptured in the course of typhoid fever. All the blood-vessels found at the edge of the solution of continuity contain red corpuscles, which are well preserved if the lesion is recent, and granulo-fatty if old. When blood is thus effused into muscle it seems to be easily absorbed. The muscular movements certainly exercise a great influence on the intra-muscular lymphatic circulation, and consequently on the transportation of substances derived from the transformation of extravasated blood; but hitherto the successive stages of this absorption have not been followed, neither in man nor in animals. We know, however, that severe contusions, accompanied with considerable intra-muscular hæmorrhage, may heal in a few days, without leaving any trace. As to the changes of the blood, they do not differ from those already described in hæmorrhage of the connective tissue; the

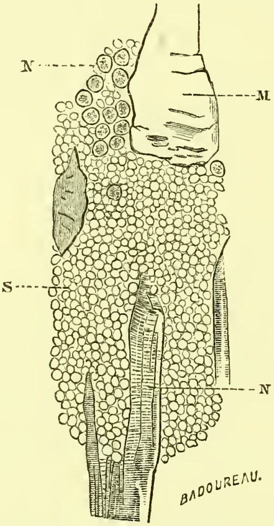

Fig. 229.—Ruptured Rectus Muscle with Hæmorrhage, in Typhoid Fever.

s, effusion of blood between dissociated muscular fibres; *m*, a muscular fasciculus in a state of vitreous degeneration; *n*, dissociated muscular fasciculus.

blood undergoes the usual metamorphoses, it then coagulates, after which it is decomposed, the fibrin is dissolved, or becomes disintegrated into very fine particles, which are taken up by the circulation.

The mechanism of muscular hæmorrhage varies according to its cause. When it is the result of direct traumatism, such as rupture of a muscle, fracture of a bone, contusion, etc., the torn vessels allow the blood to escape till it coagulates and occludes the divided vessels. Muscular hæmorrhage may also be related to obliteration and thrombosis of the veins; in such cases the arterial pressure transmitted to the capillaries is sufficient to cause their rupture. But obliteration of the arteries either by thrombosis or emboli cannot cause intra-muscular hæmorrhage, any more than ligature of an artery. The mechanism of muscular hæmorrhages in general diseases, such as purpura and hæmorrhagic fevers, is not understood.

Embolic infarctus of muscles.—True embolic infarctus of muscles is very rarely seen. We mean by this term the change consequent on the obliteration of a muscular arteriole and its branches. This lesion differs from hæmorrhagic infarctus by the absence of extravasated blood. Embolic infarctus of muscles should also be distinguished from metastatic abscess, which will be described when considering inflammation. We have only met with two cases of muscular infarctus, which were the result of emboli from endocarditis and endarteritis. In these cases, whitish and slightly opaque masses of conical form were seen in the midst of the muscular tissue, contrasting strongly with the rest of the muscle, which was red and semi-transparent. On examining these parts microscopically the primitive fasciculi were still seen to be striated; they contained only a few pigment granules derived from the muscular hæmoglobin, but no fat granules. This pigmentary change is similar to that already described as existing in fœtuses dead before expulsion. In the case which we examined we could not assign a date to the lesion. The changes in the blood-vessels will be described when considering infarcts in general (vide Lesions of the Vascular System).

Multiplication of the nuclei of the primitive fasciculi.—As we have already shown, multiplication of the muscular nuclei is seen to be the result of vitreous change, and even of granular change, but it may sometimes occur separately. This lesion is observed in inflammation of the muscles following a wound, in the vicinity of a tumour, for example, cancroid of the lips or tongue, in certain forms of paralysis, in acute ascending paralysis, and in animals after division of a nerve. When a nerve has been divided in a rabbit, the only modification found in the muscles two or three weeks after the experiment is multiplication of the nuclei of the primitive fasciculi; they become larger, divide, and form elongated groups (Vulpian). In these groups the nuclei are arranged in series in a granular protoplasm: this is generally characteristic of proliferation of the muscular nuclei. The nuclei are contained in a common protoplasmic mass; it is only in exceptional cases that the protoplasm is seen to form distinct masses round each nucleus, as, for example, in the final stage of vitreous degeneration.

In epithelioma, multiplication of the muscular nuclei is often very marked; at the same time there is a more or less notable atrophy of the primitive fasciculi, so that the nuclei, and the protoplasm surrounding them, are much more evident than normally. As these nuclei are large and contain large nucleoli, some authors have thought that they concur in the formation of epithelial cells; but we have never observed any fact in support of this opinion. It is also far from certain that proliferation of the muscular nuclei takes any part in the formation of pus.

Inflammation of muscles or myositis.—The simplest form of inflammation of muscles, and the easiest to study, is that which takes place in consequence of wounds. If a muscle is implicated in a wound, the denuded or divided portion gives origin to granulation tissue. This new granulation tissue is developed from the interfascicular connective tissue, by the production of embryonic tissue and blood-vessels. The embryonic cells are found, not only on the surface of the wound, but between the primitive fasciculi to a depth which varies according to the intensity of the inflammation and the stage of the morbid process. In contusions such as, for example, a gunshot wound, embryonic tissue may be found in the affected muscle to the depth of many centimetres, when the wound is suppurating freely. In such a wound on the twelfth day, in a vertical section carried from its surface through the muscle, there will be found, first a layer of simple embryonic tissue, in which are loops of dilated capillaries with embryonic walls; beneath this layer, the thickness of which varies from 1 to 5 mm., is found a second, in which the embryonic tissue is furrowed by atrophied primitive fasciculi, which instead of all having the same direction, as in a normal muscle, are arranged with the greatest irregularity. These atrophied primitive fasciculi have a diameter of ·01 to ·03 mm.; in preparations obtained after maceration in a ·2 per cent. solution of chromic acid, transverse striation of the fasciculi cannot be distinguished, and they seem to be composed of fibrils separated by an exudation. The muscular nuclei, multiplied to excess, form groups or series, some of which are on the surface, others at the centre of the fasciculus; the sarcolemma seems to have completely disappeared. Round the atrophied primitive fasciculi, the embryonic tissue begins to become organised and forms a reticulum, the fibres of which, at many spots, are blended with the muscular fasciculi. In the deeper layers, the interfascicular connective tissue contains fewer cells, and the atrophy of the muscular fasciculi is more marked; they then show an increase in the number of their nuclei, which in transverse sections are seen to form a circle round each fasciculus (*vide* fig. 230).

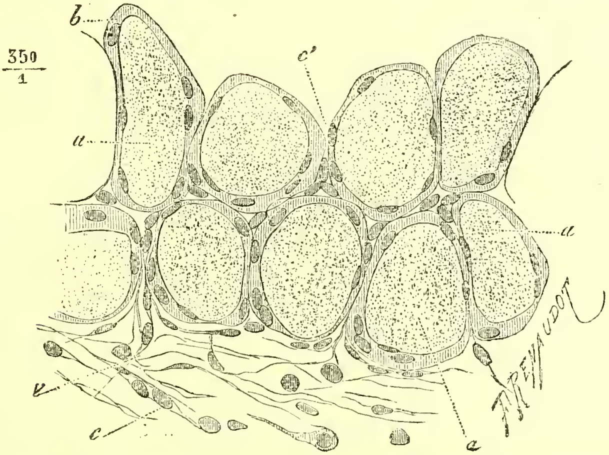

Fig. 230.—Muscular Fasciculi of the Gastrocnemius Muscle of Man from a large Contused Wound of the Calf.

Section made through the muscular tissue beneath the layer of granulations: *a*, muscular substance; *b*, protoplasm and nuclei, *c'*, situated between the sarcolemma and muscular substance; *c*, inflamed connective tissue.

It remains to be added that in many spots of the interfascicular connective tissue are found free globular cells containing brown granules of hæmatin. This fact shows that there has been an infiltration of blood into the tissue, which has been in a great part absorbed by the same process as that described in hæmorrhages of the connective tissue.

The changes described in a simple case are seen with slight variations in all cases of muscular inflammation observed in man, or in animals submitted to experiment. The muscles divided in stumps after amputation undergo the same changes. Recovery takes place definitely by the organisation of the embryonic tissue at the surface, and by the disappearance of that which is interposed between the muscular fasciculi; but this simple and natural course towards recovery may be prevented by various accidents (hæmorrhages, suppuration).

Suppuration of muscles.—Muscles suppurate in limited foci or by diffuse infiltration. The limited foci are seen as accidents in the vicinity of a wound, or they are related to purulent infection, glanders, or farcy.

The metastatic foci of purulent infection differ entirely from white embolic infarcts. They vary in size from a hemp-seed to that of a fist. The pus contains a detritus composed of connective tissue and disintegrated muscular fasciculi. The purulent focus is surrounded by a greenish brown zone, in which the interfascicular connective tissue is infiltrated with lymph cells and red blood corpuscles, and the muscular fasciculi contain proteid, fat, and pigment granules. This zone may be met with in the walls of all purulent foci of muscles, whatever may be their cause. In diffuse inflammation, which is often seen in the divided muscles of amputated limbs in patients who have succumbed to purulent infection, or in inflammation of the psoas muscle, purulent infiltration causes fatty degeneration of the primitive fasciculi ending in necrosis.

Chronic inflammation of the muscles.—This occurs as a secondary phenomenon round articulations affected with white swelling or chronic rheumatic arthritis; it is also met with in the neighbourhood of purulent fistulæ leading from carious or necrosed foci. The lesions of the interfascicular connective tissue consist in hypertrophy due to an exuberant production of cells, and to the formation of an exudation, so that the divided surface of these muscles on section, instead of presenting their characteristic fasciculated appearance, show a marbled surface in transverse sections and fibrous in longitudinal sections. The muscle has lost its colour and is whitish or pink, its firmness is increased, and it has partly lost its elasticity. The muscular fasciculi are seen to have undergone various changes; in some striation is preserved, and their nuclei are more numerous than normally; others have undergone granular or granulo-fatty degeneration; finally, in a certain number of cases, most of the fasciculi show the lesions of vitreous degeneration. Some authors refer the fibrous nodules and even the needles of bone, which are produced in consequence of repeated contusions and friction, to chronic inflammation. It is thus that Rokitansky explains bone formations in the biceps of German soldiers, and in the adductors of the thighs of riders who are accustomed to remain long in the saddle.

Rupture of muscles.—Rupture of muscles caused by contused wounds is not considered here, but only those ruptures which are caused by muscular contractions. If the muscle is healthy, there must have been considerable strain to produce rupture, which is, however, not the case if the muscle is in a morbid condition. In acute typhoid fever, for example, when the muscles are degenerated, the rectus abdominis may be ruptured by the simple effort of sitting up in bed. This rupture has been more particularly studied anatomically, for other muscular ruptures are generally followed by recovery. Rupture of the rectus abdominis in typhoid fever often occurs without the physician being aware of it, the lesion being only discovered on the post-mortem table. It is then seen to have occurred in an irregular manner, so that the surface of the divided fragments is uneven, the space between them being occupied by a dark brownish-red blood-clot, marked with opaque whitish lines. On dividing the muscle longitudinally, a brown stain and rigidity are found at the solution of continuity, to the depth of from one to many centimetres. The blood-clot is formed of red corpuscles contained in a fibrous reticulum, and shows the various changes observed in interstitial hæmorrhage; in the white lines, fibrin and white corpuscles are found chiefly. At their point of division the muscular fibres show very advanced granulo-fatty degeneration (*vide* fig. 229). Between the muscular fasciculi, the connective tissue is infiltrated with coagulated blood, with which the blood-vessels are also filled. On comparing the muscular fasciculi near the rupture with the fasciculi of the same muscle far removed, only a small number of the latter are found to be in a state of fatty degeneration, while many have undergone vitreous degeneration; near the rupture, on the contrary, the fasciculi contain a great number of fat granules; it is hence highly probable that fatty degeneration is at least in a great part consecutive to the rupture.

III. Tumours of the Muscles.

Sarcoma.—We know of no case of primary sarcoma of the muscles, but extension of sarcoma into muscle is frequent. Fasciculated sarcoma is the most common, but embryonic or encephaloid sarcoma, lipomatous, mucous, erectile, and melanotic sarcoma are also observed. It is unnecessary to redescribe these different tumours, which in muscular tissue present the usual characters (*vide* chapter on Tumours). The morbid mass always develops from embryonic tissue, previously formed in the interfascicular spaces. The new tissue compressing the primitive muscular fasciculi causes them to atrophy, which may be simple or accompanied with granulo-fatty degeneration: the latter is principally met with in those cases in which the formation of sarcomatous tissue has been very rapid. It is also observed in exuberant callus implicating muscular tissue, which at a certain stage of its development shows the structure of sarcoma.

Fibroma.—Simple fibroma of muscles is generally the result of mechanical irritation; these tumours, once established, do not increase, nor cause any marked disturbance of muscular function; at least if those cases of muscular atrophy with increase of fibrous tissue between the muscular fasciculi are not considered to be primary fibromata; but in these fibrous formation is a secondary phenomenon.

Myxoma and **lipoma** are met with in muscles as separate tumours, or as compound tumours, called lipomatous myxomata. They are most frequent in the muscles of the tongue, lips, and buccal walls, but they may be met with in other muscles of the body.

Gummata of the muscles, though rare, are well known clinically. They have not however been made the subject of thorough histological examination.

Tubercle.—Tubercular ulcers of the tongue and pharynx are not rare. In the midst of the muscular fibres at the base or edges of these ulcers, tubercular granulations are always met with; which, in sections cut after hardening in alcohol or alkaline bichromates, are seen to be quite characteristic. In them may be recognised giant cells and masses of small cells pressed together in the form of nodules, as well as obliteration of the blood-vessels in the nodules. Finally, discrete or confluent tubercles may be found in different states of caseous degeneration; when confluent, they form caseous masses visible to the naked eye.

Carcinoma.—Carcinoma of the muscles is always secondary; it is produced by extension, or by infection; it is developed in the interfascicular connective tissue, where it shows the usual phases of evolution, while the primitive fasciculi undergo simple atrophy with multiplication of their nuclei, or atrophy with fatty degeneration. Encephaloid or scirrhus are more often met with in muscles, but the other varieties of carcinoma may also be found; we may notice, in particular, the extension of scirrhus of the breast to the pectoral or intercostal muscles, and extension of encephaloid of the uterus to the psoas-iliacus muscles, etc.

Epithelioma.—Epithelioma of the orbicularis oris occurs almost invariably in cancroid of the skin and labial mucous membrane. It is in this situation that the opportunity is most frequently given of studying the development and growth of epithelioma in muscular tissue. Long before the epithelial buds have advanced between the primitive muscular fasciculi, a development of embryonic tissue may be observed in the interfascicular connective tissue separating the bundles: some of the fasciculi may remain grouped, but they are very few in number, and their nuclei are always seen to enlarge and multiply, while the muscular substance gradually atrophies, its characteristic striation being preserved. The epithelial buds advance into the substance of the muscle in the midst of the embryonic tissue developed between the fasciculi. The tongue is attacked in the same way in epithelioma of this organ. These tumours are of the lobulated variety. Tubular epithelioma, developed primarily in the antrum Highmori or the nasal fossæ, may also extend to the muscles of the face, and give origin there to diffused or circumscribed masses. Epithelioma may by extension or metastasis invade other muscles, notably the heart.

Chondroma sometimes invades the intermuscular connective tissue, as may be seen sometimes in chondroma of the parotid.

Osteoma of the muscles caused by mechanical irritation has been already described (*vide* p. 453): we may add that, in the vicinity of an articulation affected with long-standing chronic inflammation, osseous growths may be often seen in the tendons, and which extend to the muscles and form nodules or spiculæ in the substance of the muscular tissue.

Angioma, either simple or cavernous, is not very rare in muscles; it must not be confounded with varices.

IV. Parasites of the Muscles.

Three varieties of parasites are observed in muscles—cysticerci, echinococci, and trichinæ.

Cysticerci are rarely met with in human muscles: they do not generally cause accidents during life, and are hence only discovered on post-mortem examination. We have had the opportunity of examining the muscles of a cadaver, in which the cysticerci were contained in whitish cysts, the size of a pea, situated between the muscular fasciculi, and surrounded with a fibrous shell. The cysticerci were infiltrated with calcareous granules, but their heads, suckers, and hooklets could nevertheless be found.

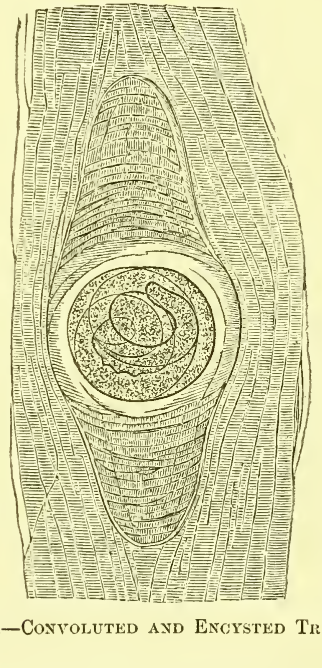

Fig. 231.—Convoluted and Encysted Trichina.

There are a few cases on record of hydatid cysts with echinococci in muscles, the microscopical characters of which were indisputable.

Trichina (*Trichina spiralis*), discovered by Owen in the muscles, is found in the form of a small convoluted worm, contained in a cyst. These cysts, which are oval or egg-shaped, are situated in the interior of the muscular fasciculi, or in the interfascicular connective tissue: they are hardly visible to the naked eye; they possess two envelopes, one formed by the sarcolemma or connective tissue, the other belonging to the animal; they contain one, two, or three convoluted trichinæ of characteristic form. If they remain long in the organism, the cysts undergo calcareous infiltration, and the worms become brittle. The adjacent muscular fasciculi undergo granular change, and the irritation resulting from the presence of the cyst determines a new formation of blood-vessels round its edge.

Trichinæ are asexual in the muscles, but when swallowed by a mammalian they become free and attain sex in the digestive canal.

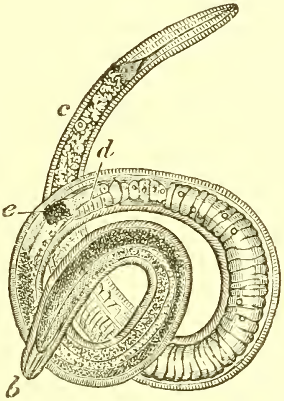

Fig. 232.—Trichina arrived at Complete Development.
c, cephalic extremity terminating by the œsophagus and mouth; *b*, caudal extremity terminating by the anus; *e*, genital organs.

The males are 1·5 mm. in length, the females 3 mm. Their anterior extremity is pointed: it contains the œsophagus, and terminates by a mouth. The posterior extremity is blunt and rounded; the sexual organs are simple, and are situated in the middle third of the body; the testicle is in the posterior third. Copulation takes place in the intestinal canal, and a few days afterwards the female produces a large number of young. These perforate the intestinal walls and distribute themselves throughout the economy, locating themselves finally in the striated muscles, with the exception of the heart. They are arrested in their migration by the insertion of the tendons. Encysted in the muscles, they produce the various changes described above.

CHAPTER VII

THE BLOOD

The Pathological Histology of the Blood.

ALTERATIONS of the blood in disease are numerous; they may almost all be ascertained by means of chemical analysis, only a few of them can be recognised by the microscope; it is with the latter, however, that we are concerned. The histological changes of the blood consist in variations of the number of white and red corpuscles, in the decrease of hæmoglobin contained in the red corpuscles, in variations of size of these elements, and in the change of resistance of the red corpuscles: finally, bodies may be found in the blood which do not exist there normally.

Changes in the number of the corpuscles can be only appreciated by means of the direct methods of numeration (*vide* p. 48). An increase in the globular richness of the blood may be due, either to an actual increase in the total number of corpuscles, or to a loss of fluid resulting from concentration of the blood; as, for example, after profuse perspiration, diarrhœa, etc.

Estimation of the hæmoglobin.—The red corpuscles do not always contain an equal quantity of hæmoglobin; this has been proved by the researches of Duncan, Malassez, and Hayem. Malassez and Hayem have attempted to give an idea of the quantity of hæmoglobin contained in each corpuscle. To ascertain this the quantity of hæmoglobin must be divided by the number of corpuscles contained in a given volume of blood. As chemical processes require too large a quantity of blood, recourse is had to colorimetric methods.

The method of Hayem is derived from that of Welcker; it consists in comparing a certain thickness of a given solution of blood with a series of conventional tints. The depth of the tint corresponds to a blood containing a certain determined number of normal red corpuscles; the tint 5, for example, is equivalent to 4,000,000 normal red corpuscles. A blood which in solution would give this tint should have as much hæmoglobin as if it contained 4,000,000 red corpuscles per cubic millimetre. On dividing the number of corpuscles giving this tint by the number of corpuscles given by numeration, the relative proportion is obtained between the colour of a normal red corpuscle and that of the blood examined. If, for example, it is found that by the tint, 4,000,000 is the number of red corpuscles, and by numeration 5,000,000, the corpuscle only contains 0·8 of the hæmoglobin it should contain normally. This method is inconvenient in many ways; the colorimetric scale is difficult to produce mechanically, and thus is not found in commerce; the unit chosen is arbitrary; and, finally, the results are expressed by the relative quantity, and not by the absolute amount of hæmoglobin present.

The apparatus of Malassez is composed of a screen, which the observer places between himself and the light. The screen is pierced by two apertures placed near together; behind one of the apertures is placed the bulb of a Potain's mixer, containing the solution of blood (the ordinary bulb is modified for this purpose, and has two plain and parallel surfaces); behind the other aperture is a coloured prism, containing a solution imitating blood in colour (in the spectrum it gives two bands closely resembling those of reduced hæmoglobin). This prism is moved up and down by means of a screw, so that the parts, of variable thickness, and hence more or less deeply tinted, are passed before the aperture of the screen, until the tint is found exactly corresponding to that of the solution of blood in the mixer. On one side of the prism is a graduated scale, which passes in front of a fixed needle, which indicates the degree of the scale corresponding to the blood examined; on referring the number obtained to a table gummed on the screen, the richness of the blood examined per cubic millimetre is ascertained. The scale has been established by means of series of examinations of solutions of blood accurately measured. Though this method is not rigorously exact, no more than any other colorimetric method, it is more than sufficiently precise for clinical needs. After having determined the proportion of hæmoglobin contained in the red blood corpuscles, it would be well to ascertain the quality of this hæmoglobin: certain facts seem to show that it undergoes changes, so that equal weights of hæmoglobin do not absorb equal quantities of oxygen.

Changes in the size of the corpuscles.—The blood corpuscles show changes in size, which, in the red corpuscles, is a very interesting subject of study, when considered in connection with their modifications of number and colour. Numeration and colorimetry teach us, for example, that the red corpuscles of chlorotic patients contain less hæmoglobin than normal corpuscles; this is not owing to the fact that they are smaller, for on measurement they are found, on the contrary, to be larger than normal; the change in the corpuscles is in the corpuscular substance itself, in that it is less rich in hæmoglobin.

Mensuration of the corpuscles is not without difficulty, by reason of their small size, their mobility, and the great number of processes necessary to arrive at a reliable mean. The following is the process recommended by M. Malassez; a drop of blood is deposited on a slide and spread out into a very thin layer, which is fixed either by rapid dessication or by exposing it in the vapour of osmic acid. The preparation is then drawn by aid of a camera lucida, a lens being used, the magnifying power of which has been accurately determined beforehand by means of a micrometre. The diameter of each outlined corpuscle is then measured with a compass, and the lengths thus obtained are placed end to end on a horizontal line, traced on a sheet of paper: the total length first divided by the number of corpuscles, then by the magnifying power,[1] gives the mean diameter of the corpuscles. The thickness of the corpuscles, less often sought for, is obtained in preparations of fresh blood by drawing straight rouleaux of corpuscles, and dividing the height of the pile by the number of corpuscles composing it.

Changes in the resistance of the corpuscles.—In the presence of certain reagents the red corpuscles show changes in their power of resistance. In a preparation of normal blood diluted with artificial serum, some corpuscles are seen to preserve their biconcave form for a long time, while others change rather rapidly, and become either crenated or spherical. In the pathological condition, these phenomena are often very marked, either in one direction or the other, even when the nature of the serum used, the strength of the dilution, and the time of the observation are exactly the same. In anæmia from lead-poisoning, for example, the red corpuscles show great resistance, while in chlorosis they alter and become granular with great rapidity. Such alterations may have a marked influence on general nutrition, and it is most important that they should be studied in a thorough manner.

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[1] If a lens be selected and the tube of the microscope graduated so that the figure thrown by the camera lucida exactly magnifies 1,000 diameters, the process is much simplified. Care must be taken to correct the errors of refraction, which may be done by placing the paper at such an inclination that it is at right angles to the optic axis, as recommended by Malassez.—Tr.

We will now proceed to study changes of the blood met with in those diseases in which these alterations have a special importance.

Inanition.—In inanition, according to the experiments made on the guinea-pig and fowl, the number of red corpuscles increases at the beginning, probably by concentration of the blood; then the number diminishes and the animal dies, the normal number not being reached, or at all events hardly passed. This increase and diminution explain the contradictory results obtained by different observers. In a subject suffering from cicatricial stricture of the œsophagus, and who is ill nourished, and in animals that have undergone prolonged abstinence (frogs at the end of winter), the number of corpuscles falls below the normal. The richness of corpuscles in hæmoglobin is not always proportionate to their number (Malassez). In slow as in rapid inanition the total mass of the blood diminishes in a marked degree.

Wounds and suppuration.—In wounds and suppuration there is a more or less considerable decrease in the number of red corpuscles, due probably to concomitant hæmorrhage. In an experiment on a dog, in which a wound was produced without hæmorrhage, the number of red corpuscles was not modified (Malassez). The white corpuscles, on the contrary, rapidly increase in number. If there is no discharge of pus, nor formation of abscess, the number of white corpuscles gradually diminishes, and returns to the normal, even before the wound is completely cicatrised. Similar phenomena are observed after amputation, and after parturition; but if complications in the form of abscesses or purulent infection occur, the number of white corpuscles considerably increases, until there may be one white corpuscle to fifty-four red. Purulent collections, abscesses, empyema, etc., are also accompanied by an increase in the number of white corpuscles, which ceases as soon as the contained pus has free exit. This leukæmia or leucocythosis of suppuration may aid the diagnosis in doubtful cases of deep suppuration. In malignant pustule there is also a considerable increase of white corpuscles.

Hæmorrhage is followed by a decrease in the number of red corpuscles, more marked as the hæmorrhage is more considerable. In women the same phenomena are observed during menstruation. The quantity of hæmoglobin per corpuscle is not modified, if the hæmorrhage has been moderate and not repeated. The white corpuscles are more numerous; but it may be asked if this is a result of the hæmorrhage itself, or only of the accompanying wound. Experiments on dogs and rabbits show that a wound, without hæmorrhage, is followed by as great an increase in the number of white corpuscles as if there had been hæmorrhage, while a very insignificant hæmorrhage with a wound—blood-letting from the jugular vein with a trocar, for example—does not lead to a marked increase in the number of white corpuscles (Malassez). Hence it may be concluded that, if white corpuscles are more numerous than usual, it should be principally attributed to the wound.

Diarrhœa.—Diarrhœa and purgation are followed by an increase in the number of red corpuscles, evidently produced by the concentration of the blood. This concentration is carried to its extreme in cholera; it disappears when the loss of fluid ceases. In new-born children who are athreptic, cachectic, and affected with diarrhœa, the number of corpuscles increases; sometimes it is normal, which is doubtless due to the fact that the decrease of corpuscles caused by the anæmia is masked by the concentration of the blood due to the diarrhœa. In a man affected with malarial cachexia, and in an equally cachectic tubercular person, both the subject of diarrhœa, the number of red corpuscles is extremely small, less than 1,000,000 per cubic millimetre. Here, however, there is no contradiction, for the cachexia balances the effect produced by the diarrhœa. Perhaps diarrhœa may, in the end, produce a diminution in the number of the corpuscles, like prolonged abstinence.

Lead-poisoning.—There is a marked decrease in the number of red corpuscles in lead-poisoning; they are larger than normally, but the increase of size does not compensate for their numerical decrease, for the corpuscular mass is less in the subject of lead-poisoning than in the healthy man. In lead-poisoning the red corpuscles are preserved intact in artificial serum much longer than normal corpuscles.

Malaria.—In malaria there are many conditions of the blood to be considered; first, in simple intermittent fever, there is after each access a considerable diminution in the number of red corpuscles; repair then takes place, but, as it has not time to be accomplished before the return of the next access, the anæmia becomes progressive. As recovery is approached, the reverse is the case; the destruction of the red corpuscles is less in each access, and between the attacks the blood recovers more than it has lost. In malaria, the size of the red corpuscles is larger than normal. The white corpuscles diminish in number after each access, more so proportionately than the red. Secondly, in malarial cachexia there is diminution of the red corpuscles, and more particularly of the white. On passing an electric current through the spleen an increase of the number of white corpuscles in the blood follows, which increase disappears when the spleen returns to its normal size. Thirdly, in pernicious malaria the white corpuscles increase after each access, and at the same time melanemic granules appear in the blood. Some time after the access the white corpuscles return to the normal standard, and the melanotic granules disappear (Kelsch).

Erysipelas.—In erysipelas the number of both white and red corpuscles diminishes, the white decreasing particularly at the termination of the eruption. During convalescence the proportion of corpuscles returns to the normal; but if the erysipelas becomes phlegmonous, the number of white corpuscles increases, and only diminishes when the pus has free exit. There is also an increase in the number of white corpuscles when erysipelas attacks patients who are the subjects of scrofulous or lymphadenic hypertrophied glands. The blood taken from the erysipelatous parts is less rich in white corpuscles than that which comes from healthy parts; at the same time the serum, which infiltrates the tissues in which the erysipelas is situated, is very rich in white corpuscles, as if these elements were entangled in the parts affected with the erysipelatous inflammation.

Variola.—There is a considerable decrease in the number of red corpuscles in variola, which condition persists for a long time after recovery. The white corpuscles are, on the contrary, more numerous, particularly at the period of dessication of the pustules: they then return to their normal proportion, if complications or phlegmon do not supervene (Verstraeten).

Typhoid fever.—In typhoid fever there is a decrease of the red corpuscles, and an increase of the white during the first week; these elements return to their normal relations in the following weeks (Bonne).

Acute and chronic glanders.—In horses affected with this disease there is a characteristic increase of the white corpuscles.

Syphilis.—Immediately after the first accidents of syphilis there is a marked decrease in the number of both white and red corpuscles, particularly of the red. Moderate doses of mercury cause this anæmia to rapidly disappear (Wilbouchewicz). In syphilis of the new-born the red corpuscles are more numerous and paler than normally (Cüffer).

Cancer.—In cancer the red corpuscles are greatly diminished in number: they are also deficient in hæmoglobin, and diminished in size; but this diminution of volume is not considerable enough to explain the deficiency of hæmoglobin, which proves that the corpuscular substance is changed.

Tuberculosis.—At the commencement of tuberculosis the number of red corpuscles is not sensibly modified; but in cachetic tubercular subjects the number is much lowered, and may descend below 1,000,000 per cubic millimetre. When there is improvement of condition, the number of corpuscles increases. The quantity of hæmoglobin per corpuscle is below normal in tubercular subjects.

Rheumatism.—In acute general rheumatism, notwithstanding the profuse perspiration from which the patients suffer, and which ought to cause concentration of the blood, a marked decrease in the number of red corpuscles is found, which leads one to suppose that the actual decrease in the number of corpuscles is much more considerable than indicated by numeration. The blood returns very slowly to its normal condition. In subacute uni-articular rheumatism, decrease of red corpuscles is still very manifest. During attacks of gout the red corpuscles are found to diminish in number, to be of large size, and to show much resistance to reagents.

Interstitial nephritis and anæmia.—In interstitial nephritis and anæmia the red corpuscles are diminished in number, increased in size, and more resistant; the number of white corpuscles is increased. Injections of carbonate of ammonia and creatin into the blood will produce the same troubles (Cüffer).

Icterus.—In cases of simple icterus a marked diminution in the number of the red corpuscles has been observed (Malassez).

Anæmia.—In the anæmia of miners the number of corpuscles may be normal, and it is rare to find low figures; but the red corpuscles are paler than normally (Fabre).

Chlorosis.—In chlorosis the number of red corpuscles is sometimes normal, sometimes increased; the elements are always deficient in hæmoglobin; they are at the same time larger, which shows a profound change in the corpuscular substance since the corpuscles, though larger, contain less hæmoglobin.

Adenia.—In adenia characterised by hypertrophy of the lymphatic glands, either simple or accompanied with lymphadenomata, and in cutaneous lymphadenia (fungoid mycosis) there is no increase in the number of white corpuscles, but the number of red corpuscles may be singularly diminished.

Leucocythæmia. — Leucocythæmia (Bennet), or leukæmia (Virchow), is a disease characterised by persistent increase in the number of white blood corpuscles. Towards the termination of the disease the white corpuscles are as numerous, or even more numerous, than the red ; the blood is then of a pink colour, without having the ichorous appearance observed in hydræmia. There is always at the same time decrease in the number of red corpuscles, and this decrease may be sometimes so considerable as to make the number of white corpuscles appear larger than it really is. On examining preparations of leukæmic blood, without the addition of water, the white corpuscles are seen in the form of granular bodies, of a size varying between 7 μ and 12 μ ; on the addition of water these corpuscles swell, become more transparent, and in some is perceived a single spherical nucleus, measuring 6 μ to 7 μ, in others two or more nuclei placed side by side.

Virchow distinguishes between leukæmia with splenic hypertrophy, in which large white corpuscles, containing one or many nuclei, predominate, and that in which there is a series of ganglionic tumefactions, and where small uni-nucleated corpuscles are more numerous. Upon these different characters he bases lienal leukæmia, related to hypertrophy of the spleen, and ganglionic leukæmia, related to hypertrophy of the lymphatic glands. This distinction cannot be maintained, for, on examining the blood of a leukæmic person several days in succession, sometimes the multinucleated white corpuscles are seen to predominate, at others the uni-nucleated. We may add, moreover, that this distinction of Virchow's, founded on the analogy of the white corpuscles, with the cells of the spleen in one case, and with those of the lymphatic glands in the other, is no longer admissible. It is known, in fact, that the glands or new lymphoid organs contain in leukæmia larger elements than those of the splenic parenchyma ; further, that in leukæmic patients changes of the spleen, lymphatic glands, and other lymphoid organs are most frequently coincident ; new lymphoid organs are even frequently produced in these patients, in the form of tumours (*vide* Lymphadenoma, p. 245).

Besides the ordinary white corpuscles, some authors (Klebs, Erb) have described in leukæmia nucleated red corpuscles, which they consider as intermediate elements between white and red corpuscles. We have searched in vain for these intermediate corpuscles in the blood of many leukæmic patients, without ever meeting with them; more particularly in a case of leukæmia in the wards of M. Tillaux, in which the alterations of the blood were so marked that the number of white corpuscles exceeded that of the red, but we were unable, after repeated and minute examinations, to find a single white corpuscle coloured by hæmoglobin. Many white corpuscles, particularly the largest, contain very small spherical granules of an amber-yellow colour, grouped round the nuclei. This appearance may be explained by the destruction of the red corpuscles, particles of which have been absorbed by the white corpuscles.

Melanæmia.—By this name is signified the presence of pigment particles in the blood. This alteration, described for the first time by Frerichs, is seen when the spleen has undergone a series of congestive attacks, notably in malarial poisoning. We have met with it in Paris in the subjects of pernicious malarial fever. In the cases which we have observed, the particles of pigment present in the blood were round or angular, of a positive black colour, extremely small, of about 8 μ or 9 μ in diameter; they were either contained in the white corpuscles, or enveloped in a thin and colourless granular zone, which very probably represented the protoplasm of a white corpuscle. In post-mortem examinations of persons who succumbed, most of the organs, particularly the spleen and liver, were found of a slate colour. On making sections of these organs, after hardening the fragments in alcohol, pigment granules were seen in the white corpuscles contained in the blood-vessels, in the vascular cells, in the cells of the perivascular connective tissue, and even in the cells of the parenchyma. The splanchnic lymphatic glands were equally pigmented.

Pathological pigment behaves in the same way as an inert granular substance contained in the blood, vermilion for example. On injecting fine powdered vermilion, suspended in water, into the blood of an animal, the particles are taken up by the white corpuscles, and carried with them into the different organs; they traverse the vascular walls, become dispersed, and finally fixed in the elements, which are the seat of the pathological pigmentation. There is reason to suppose that melanæmia is produced by pigmentary transformation of the blood in the spleen, and the transportation of the pigment by the white blood corpuscles. Pigmented lymph cells are generally larger than others, and therefore liable to accumulate in some of the blood-vessels and impede the circulation. These do not cause true embolism, as Frerichs and Virchow maintain, but phenomena similar to that of stasis of the white corpuscles in leukæmia (*vide* p. 248).

Parasites of the blood.—At the present day there is reason to believe that most infectious and contagious diseases are due to the existence of microbia, which, after penetrating into the organism, grow and multiply, and are carried to the different organs by the circulation of the blood and lymph. If this is actually the case, these microbia ought to be apparent in the blood, at least during some stages of the disease. The presence, however, in the blood of definite microbia has only been assured by microscopical examination in two diseases: charbon (anthrax), and recurrent fever. The bacteridium of charbon (Davaine), *Bacillus anthracis* (Cohn), has been found by Davaine in the blood of animals affected with charbon, malignant pustule, splenic disease, etc. These microbia are found in the form of articulated and motionless filaments, which in simple microscopical observation do not differ from the bacteria developed in animal fluids, at the commencement of putrefaction; but while inoculation with these fluids has no effect, or is only followed by more or less pronounced septicæmia, inoculation with charbon blood, even when very diluted (Davaine), produces the infection of charbon. In the blood of animals which continue to live after inoculation, bacteridia are found in more or less considerable numbers. Hence we are led to look upon these microbia as the veritable agents of infection. It is true that inoculation with charbonous or anthracoid fluids produces the accidents of infection, notwithstanding their having been submitted to the agents which kill *Bacillus anthracis*—alcohol, compressed oxygen (Paul Bert). But, as the researches of Pasteur have shown, though the bacteridium is unable to resist these reagents, it is quite otherwise with its spores, which afterwards, placed in favourable conditions, reproduce the parasites. We will not here enter into the discussion which has been raised, as to whether the disease is the direct result of the presence of the parasite, or if it is produced by a virus which is formed and developed simultaneously with the bacteridia. Though the data hitherto collected induce us to lean towards the first of these hypotheses, that of direct parasitic action, which is Pasteur's opinion, it must nevertheless be remembered that it is not yet established on an indisputable basis.

In the blood of persons affected with recurrent fever, Obermeier has found another microbium, also belonging to the family of Schizomycetes of Nægele, which instead of consisting of rectilinear rods, like the Bacillus, is spiral. This is the *spirillum Obermeieri*. Extremely thin, the spirillum of recurrent fever has a length of one and a half to five times greater than the diameter of a red blood corpuscle: while the bacteridium of charbon is motionless, the spirillum of recurrent fever moves about in the preparation, turning over and over. It is not known if it is a distinct species, or if it belongs to the same species as the spirillum discovered in water by Ehrenberg, or as that which exists normally in the mouth. All these questions still require study. It will be understood that we cannot give them a larger space in an elementary manual, which ought only to contain facts completely established.

The **filaria sanguinis hominis** is a parasite existing in the blood in immense numbers. Researches into the life-history of this hæmatozoon have been made, within the last few years, by Bancroft, Lewis, Cobbold, Manson, and Stephen Mackenzie, and it has been satisfactorily proved that filaria is the cause of elephantiasis and chyluria. The filaria sanguinis is the embryo of a worm first discovered by Bancroft in Australia in 1876, and called by Cobbold the *filaria Bancrofti*. This parasite inhabits a lymph channel in the human body, and has been found *in situ* by Manson. (*Trans. of the Path. Soc.* Lond. 1881.) A male and female live together; the female is a long slender hair-like animal, three inches in length, and $\frac{1}{100}''$ in breadth; it is semi-transparent, and while lying in the tissues is animated by wriggling movements; the male is smaller. Manson contends that the filaria is vivaporous, and that the ova found in the lymph are aborted specimens. The filariæ are transparent, structureless, snake-like worms, $\frac{1}{3500}''$ in diameter, and move about with great activity. They are absent from the blood during the day, but as the night advances they appear and increase rapidly, and may number 100 or even more in every drop of blood, decreasing again as the day approaches. Dr. Stephen Mackenzie found in a recent case under his care in the London Hospital (*Brit. Med. Jour.* Oct. 22, 1881) that on reversing the habits of his patient, and turning night into day, the filariæ were found during the daytime and disappeared at night. The ovum measures about $\frac{1}{600}''$ in diameter, nearly six times larger than the embryo, which is simply the ovum stretched out; it is too large to pass the lymphatic glands, and being inactive it acts as an embolus, and produces lymph stasis. Dr. Manson of Amoy has traced the double generation of filariæ, and states that the embryos are abstracted from the human body at night by mosquitoes; in the stomach of this animal they mature, and at the end of five or six days show a definite structure; on the death of the mosquito they pass into the water of the wells and rivers, which, being drunk by men, the parasite enters the human stomach. It then bores its way into a lymphatic vessel, and passing against the current become finally located in a distant lymphatic vessel. In South China, where filaria is endemic, the hæmatozoa would be found between sunset and sunrise in the blood of 10 per cent. of the native population. In a large proportion of cases the parasite gives rise to no accidents whatever, but Dr. Manson, in an able paper (*ut supra*), seeks to demonstrate that all the phenomena of elephantoid disease may be explained by infarction of the lymphatic glands by the aborted ova of the parent worm.—TRANSLATOR'S NOTE.

CHAPTER VIII.

MORBID CHANGES IN THE HEART.

The anatomical changes in the three constituent parts of the heart, the pericardium, the myocardium, and the endocardium, will be successively considered.

I. Lesions of the Pericardium.

Hæmorrhage.—Hæmorrhage into the pericardium is of two kinds: first, ecchymosis of the membrane; secondly, hæmorrhage into the pericardial cavity. Ecchymoses are more frequent in the visceral than in the parietal layer; when recent, they appear as lenticular spots, of an uniform red colour; they are sometimes confluent, forming extensive areas with sinuous margins; they are seen in asphyxia from whatever cause, in leucocythæmia, purpura, scurvy, etc., or they complicate inflammatory lesions of the pericardium, in which case they properly belong to hæmorrhagic pericarditis. Hæmorrhage into the pericardial sac is consecutive to inflammation or to rupture of the heart, or a large vessel covered by the visceral layer of the pericardium; for example, rupture of an aneurism in the ascending arch of the aorta.

Dropsy of the pericardium.—The quantity of fluid found in the pericardium twenty-four hours after death always exceeds thirty grammes; if the fluid is much more abundant, as is observed particularly in general dropsy, there is said to be dropsy of the pericardium. In this fluid are found lymph cells and epithelial cells detached from the serous membrane, isolated or in flakes, and which almost always contain fat granules. In pericardial fluid which is normal or more abundant than usual, articulated and motionless bacteria of exceptional size are frequently found. We draw no conclusion from this fact regarding their genesis. Gas is sometimes present in the pericardium of subjects in which the process of putrefaction has already commenced: it must not, however, be concluded that these gases have been present during life, and the existence of a morbid pneumatosis be assumed.

Inflammation of the pericardium. Pericarditis.—Fibrinous inflammation of the pericardium does not differ from fibrinous inflammation of other serous membranes, except by the naked-eye appearances of the solid exudation. It is most frequently general over the whole extent of the pericardium, but it may also be limited, particularly at the base of the heart, to the origin of the aorta and large vessels. The exudation is deposited on both surfaces of the pericardium, in a layer which is papillary in appearance. They are not true papillæ, for the connective tissue and blood-vessels of the serous membrane take no part in their formation; this may be ascertained by detaching the false membrane, which is smooth at its union with the pericardium. The solid pseudo-membranous exudation is solely composed of fibrin, cells derived from the endothelium, and pus cells. The papillary filaments on its free surface have been compared to the papillæ on the tongue of a cat; they are more or less flat or elongated, and their form is very variable; they are even observed when the layer of fibrin is extremely thin; they are produced by the movements of the heart in the pericardium, when the fibrin is undergoing coagulation. As to the formation of fibrin, we refer the reader to what has been said on inflammation of the serous membranes in general (*vide* p. 422). In pericarditis of many days' standing, old dilated capillaries may be already found at the base of the fibrinous projections, or newly formed capillaries. These vessels are then surrounded by a variable quantity of embryonic cells. As to the exudation itself, it contains, besides fibrin, cellular elements, white corpuscles, and cells of various shape derived from the endothelium. Fibrinous pericarditis occurs in acute articular rheumatism, pneumonia, scarlatina, variola, Bright's disease, and in abscesses of the neck and mediastinum.

Hæmorrhagic pericarditis is met with in tuberculosis, cancer of the lungs, and in cachectic disease. It differs from the preceding only by the presence of red corpuscles in large numbers, or the products of their decomposition, hæmatin and hæmatoidin, in the fluid and solid parts of the exudation. In this disease the limitation of the serous membrane and the exudation is not defined, as in simple pericarditis; dilated blood-vessels with embryonic cells penetrate the serous membrane and form loops in the fibrinous exudation; they are surrounded with embryonic cells, and they produce hæmorrhages in the exudation itself.

In **tubercular pericarditis**, in which hæmorrhages are frequent, the tubercular granulations are formed in the substance of the pericardium, or in the vascular parts of the exudation. When the pericardium and exudation are invaded by a great number of tubercles, caseous degeneration of the exudation may occur. It may then become partly detached and form, together with blood clots undergoing retrogressive metamorphoses, grey or ochre-coloured irregular masses, which are free in the cavity of the pericardium. Under the microscope are found fat and hæmatin granules, and crystals of hæmatoidin, and, if the disease is chronic, calcareous granules. In certain cases of chronic tubercular pericarditis a thick layer of embryonic tissue, studded with tubercular granulations, is found on both layers of the serous membrane. In a case which we examined, these two layers of granulations were united by a layer of fibrous tissue which had been long formed; the tuberculosis of the pericardium was primary, and accompanied only with a recent eruption of discrete tubercle in the left pleura.

Purulent pericarditis is more rare than the preceding; it is characterised by the presence of a large quantity of pus, which gives to the fluid parts of the exudation a creamy appearance, and makes the false membrane opaque. This purulent exudation may undergo caseous and calcareous degeneration like hæmorrhagic exudations.

Adhesions of the pericardium, in consequence of inflammation, are not very frequent, particularly on comparing them with those of the pleura. Incomplete adhesions are characterised by laminæ or filaments of vascular connective tissue, and are usually located at the base of the heart, between the visceral and parietal layers near the aorta and large vessels; they are also found at the apex of the heart. *Complete adhesion* of the pericardium annihilating the cavity may be seen in consequence of acute pericarditis, chronic pericarditis, or tuberculosis of the pericardium. It is most frequently impossible to ascertain the existence of these adhesions during life, and when found by chance at post-mortem examinations it is often difficult to assign them a cause. Among lesions resulting from pericarditis, or as a form of subacute or chronic pericarditis, may be enumerated the small and wart-like vascular projections, or the projecting plates composed of lamellar connective tissue, which are found on the visceral layer, particularly at the origin of the aorta and the auricles. These growths are often covered with thin layers of fibrin. This tissue of new formation may, as we have already pointed out, undergo stony change in the pericardium as well as in other organs; a calcareous carapace is then formed of variable extent, and which often sends processes into the substance of the cardiac muscle. Most frequently the calcareous plate is not exposed in the cavity of the pericardium, but is covered by a delicate layer of fibrous tissue.

Milky patches have been considered by most authors as having an inflammatory origin; they are generally smooth, opaque, and pearly; they usually form a slight elevation upon the surface of the membrane, and are particularly found on the anterior surface of the ventricle. They are very variable in size, and have irregular sinuous borders; they are very frequent (45 in 150 autopsies: Bizot), and are composed of lamellar connective tissue and elastic fibres.

Primary carcinoma of the pericardium is very rare. Förster has seen a single example of it. Secondary carcinoma is, on the contrary, rather frequent; it grows into the pericardial cavity in the form of nodules, causing pericarditis which is generally hæmorrhagic.

II. Lesions of the Myocardium.

Atrophy.—Atrophy of the heart is met with in cases of general atrophy of the muscles of the economy; in cachectic diseases of long duration, as in phthisis or at the end of typhoid fever, etc. The form of the heart is not modified when atrophy is general. The coronary arteries, which do not participate in the atrophy, are tortuous and prominent; at certain points in their course the visceral pericardium forms a membrane over them. Atrophy may be so marked that the visceral layer of the pericardium is wrinkled. Great authorities on pathological histology—Förster among others—affirm that in atrophy there is a diminution of the size of the muscular fibres; but this is extremely difficult to appreciate, owing to their great variations in diameter in the normal condition.

Atrophy of the heart may be observed, accompanied with an abundant formation of adipose tissue under the visceral pericardium, so that, though the cardiac muscle is atrophied, the heart appears at first sight to be normal in size; but on dividing the organ with a scalpel, the sub-pericardial adipose tissue is found to be considerably thickened, and from it are sent out irregular prolongations between the fasciculi of the myocardium. This lesion resembles in every way adiposity of the voluntary muscles. The degree of the lesion varies ; sometimes the atrophy is so pronounced that the muscular power of the ventricles is much reduced.

Hypertrophy.—Hypertrophy of the heart is generally related to exaggerated action in disease of the valves or large vessels, when increased force is required to overcome an obstacle to the blood current. It most frequently affects only one ventricle, the left, for example, in lesions of the aortic orifice. Traube referred hypertrophy of the left ventricle in atrophy of the kidney to the same cause. The coincidence of hypertrophy of the left heart and atrophy of the kidney is incontestable; but the explanation of Traube is nevertheless open to discussion, for it is difficult to understand how a hindrance to the circulation in so small a number of blood-vessels could produce so marked an increase of action on the part of the heart.

Hypertrophy is general or partial. The shape of the heart is not notably modified in general hypertrophy ; in hypertrophy of the right ventricle the apex of the heart is large and blunt, being composed of the apices of both ventricles, which are then at the same level. In hypertrophy of the left ventricle the apex of the heart is, on the contrary, entirely formed by itself. Thickening of the endocardium is constantly observed in hypertrophy of the heart, and to it is due some of the induration and rigidity of the cardiac walls.

The muscular fibres of the hypertrophied parts show no lesions of nutrition, or they may have undergone fatty or pigmentary degeneration. It is not known at present if hypertrophy is entirely due to an increase in size of the muscular fibres of the heart, or to a new formation of these fibres. The phenomena of the development of new muscular fibres have, however, never been observed in cardiac hypertrophy, so that the first of these hypotheses is the more probable ; it rests on the observations of Förster, who asserts that in cardiac hypertrophy the primitive fasciculi are increased in size.

Fatty degeneration.—Of all the muscles of the organism, the heart is that which most frequently undergoes fatty degeneration. When all the muscles of the body are subjected to the same influences capable of producing fatty degeneration, the heart may be alone affected. This is what occurs in the fœtus which remains a week in the uterus after it has died ; the voluntary muscles do not contain fat granules, while the cardiac fibres are filled with them. Important changes are, however, found in the voluntary muscles ; the colouring matter is separated in the form of pigment granules, which are located under the sarcolemma in the protoplasmic substance of the primitive fasciculi.

Fatty degeneration of the heart may be found in atrophy and hypertrophy, in poisoning from phosphorus or arsenic, in acute diseases such as typhoid fever, variola, leucocythæmia, etc., and in endocarditis and pericarditis ; it may be present throughout the whole of the myocardium, or be only partial. The altered parts appear to the naked eye to be grey or yellowish, and slightly opaque, clearly distinguished from the healthy parts, which are slightly translucent and of a more positive red colour ; but it must not be thought that fatty degeneration can always be recognised with the naked eye, for occasionally the opinion formed *à priori* is not confirmed on microscopic examination. The muscular fasciculi present very varied degrees of granulo-fatty change ; sometimes only a few fine granules are perceived scattered through all the fasciculi, but which do not completely hide the striations ; at others the change is so advanced that the cardiac fasciculi resemble cylinders formed entirely of fat granules.

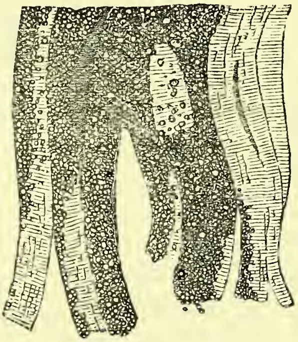

Fig. 233.—Muscular Fibres of the Heart partially degenerated, from a case of Phosphorus Poisoning.

Pigmentary degeneration.—In adult and old age yellow granules, the nature of which is unknown, are often found round the nuclei of fasciculi of the heart in the normal condition. From their colour it has been thought that they are formed of a pigment derived from muscular hæmoglobin. In chronic diseases producing marasmus, and in feeble old age, the atrophied heart is seen to be of a brown colour, and its muscular fasciculi contain a much larger number of these peculiar granules than in the normal condition; the dark colour is due to their presence. In simple melanosis, pigmentary infiltration of the heart is seen, differing from the preceding by the black colour of the granules, by their location in the connective tissue and muscular tissue simultaneously, and by the limitation of the degeneration to points or small areas (*vide* p. 315).

Hæmorrhage of the myocardium.—Congestion of the myocardium may exist during life, and be simply surmised after death. Hæmorrhage, on the contrary, leaves evident traces. It generally occurs in the form of ecchymotic spots on the external or internal surface of the heart. Ecchymoses are most frequently produced in diseases which terminate by asphyxia—diseases of the heart or lungs—and in certain cases of poisoning—by phosphorus, arsenic, etc.; and in leucocythæmia, purulent infection, and puerperal fever. The blood effused between the muscular fibres of the heart soon undergoes coagulation, so that hard nodules of a red or brown colour are formed; the muscular fasciculi included in these nodules undergo fatty degeneration. Sometimes at autopsies blackish spots are unexpectedly found in the myocardium, which were probably caused by old hæmorrhages, since the interfascicular connective tissue is found in these spots to be infiltrated with pigment granules, and the muscular fasciculi are equally pigmented.

Profuse cardiac hæmorrhage occurs in consequence of ruptures of the myocardium, which may be primary, or the result of fatty degeneration or aneurisms. Rupture due to fatty degeneration is simple or multiple; Andral reports a case in which there were five distinct rents in the myocardium. The rent is always from within outwards, and of irregular shape; if death is not instantaneous the blood infiltrates and separates the muscular fasciculi, causing diffused interstitial hæmorrhage. If the rent does not extend as far as the pericardium, an aneurism is produced, diffuse at first, but which may become circumscribed later; but most frequently the pericardium is also torn, in which case the pericardial cavity is, after death, found filled with partially coagulated blood. In a heart in which such a rupture has occurred, fatty degeneration of the muscular fasciculi will invariably be found, and the degeneration is always more marked in the vicinity of the hæmorrhagic focus.

Aneurisms of the heart are principally seen in the ventricular septum and at the apex of the left ventricle. Aneurisms of the septum and base of the heart are generally the result of the extension of a valvular aneurism; those at the apex of the heart —the most frequent of all—are probably the result of fatty degeneration, or a combined inflammation of the endocardium and myocardium; but all the phases of development of the aneurismal sac cannot be followed in this situation as in the aorta, whence it is only by conclusions drawn from analogy that the mode of their formation can be understood.

Aneurism of the apex of the heart is in the form of a sac, varying in size from a nut to that of the heart itself. When the sac is very small, it may be said to be contained in the substance of the cardiac wall, and is only diagnosed on opening the heart. The communication between the ventricle and the sac of the aneurism is by means of a large funnel-shaped opening, or by a ring-like orifice. The wall of the aneurism is rigid, so that the aneurismal sac is not emptied at the moment of the ventricular systole; stasis is nevertheless not so complete as to produce laminated clots, as in aneurisms of the aorta. At the autopsy, recent fibrinous clots are most frequently found in the sac, but when the aneurismal sac is anfractuous, dense fibrinous clots are seen adherent to the wall. The internal surface of the aneurismal sac is generally smooth; sometimes it is irregular and anfractuous.

In order to examine the wall of an aneurism under the microscope, portions are removed and fixed with pins on to a sheet of cork, and then dried. It is better to immerse the specimen in alcohol for a few days before submitting it to dessication. Delicate sections are then cut in different planes, stained with carmine, washed and mounted in glycerine to which acetic acid has been added. In these preparations are observed collections of flat cells, which seen sideways seem to be thin and fusiform, owing to their centre being swollen by the nucleus; they are separated by bundles of connective tissue and blood-vessels. The wall of the aneurism may be entirely formed of this tissue, but it is most frequently found only on the internal surface of the sac, muscular fibres grouped in small bundles, or isolated in the midst of collections of small cells, being found on the external surface.

In fresh specimens, the cells may be obtained by scraping, and may be examined on all sides. They closely resemble the cells of adult connective tissue, of which fact we have felt no doubt since

N. Pelvet made a remarkable research on this subject in our laboratory. When these cells float freely in the fluid of the preparation, they successively present edges, surfaces, and folds, by which they are recognised as flat cells of extreme thinness; their outline is sinuous, and they send out processes which are flat like the body of the cell. The shape of these cells, their arrangement in collections parallel to the internal surface of the aneurism, are due to the pressure exercised by the blood. The same cells and the same tissue are found in aneurisms of the arteries, for they are produced whenever the blood in circulation is brought into contact with newly formed layers of connective tissue.

Aneurisms produced by extension of valvular aneurisms (p. 484) are generally diffused, or the sac is very anfractuous and contains irregularly arranged clots. These aneurisms, which are generally located in the interventricular septum, bring about its destruction, and communication between the two ventricles. The tissues are torn or separated, so that shreds are pushed into the right ventricle. The muscular fibres bordering these aneurisms, the direction of which is generally slanting, are torn and show granulo-fatty degeneration.

Inflammation of the myocardium.—We do not consider myocarditis to be characterised by fatty degeneration of the muscular fibres of the heart; for this degeneration may exist in a number of cardiac affections or general diseases, which have nothing in common with inflammation; on the other hand, fatty degeneration of the muscular fibres is not observed in those cases of myocarditis, which are characterised by increase of the connective tissue of the myocardium. Muscular fibres only undergo fatty degeneration in myocarditis when they are compressed by exudations or pus cells, as, for example, in abscess of the heart; in which case the fatty degeneration does not differ from that observed in hæmorrhage of the heart. This leads us to positively deny the existence of the parenchymatous myocarditis of Virchow, which is essentially characterised by fatty degeneration of the myocardium. Myocarditis may be produced by extension of endocarditis and pericarditis, or as a symptom in purulent infection —puerperal fever, pyæmia—when it is characterised by intra-muscular abscess.

Abscess of the heart is very rare; it varies in size from a pin's head to a nut. The pus is either deposited between the muscular fibres, or it is encysted within a zone of embryonic tissue. In the first case, the muscular tissue in the vicinity of the abscess is slate-coloured; the pus contains the debris of muscular fasciculi when the suppurative inflammation is recent. In the slate-coloured zone surrounding small non-cysted abscesses are found muscular fasciculi filled with fat and pigment granules, and separated from one another by pus cells, blood corpuscles, and brown granules.

Encysted caseous masses are sometimes met with in the midst of the muscular tissue of the heart. Förster thinks they result from the metamorphoses of old abscesses. There are a few cases on record of anfractuous cavities hollowed in the cardiac muscle and opening into the left ventricle. These cavities have been regarded as abscesses, which have opened and discharged their contents into the torrent of the circulation; but at the present day these cases are interpreted as being aneurisms following endocarditis.

Interstitial myocarditis, or cardiac sclerosis, is much more frequent than was formerly supposed; it is often observed in cardiac hypertrophy, and particularly in interstitial nephritis.[1] The newly formed fibrous tissue, which is developed between the muscular fasciculi, is generally continuous with the deep layer of connective tissue of the endocardium, thickening of the latter being also often observed. Connective tissue, composed of fibres and cells, is also found, particularly round vessels, arterioles, and small veins, the tunica externa of which is thickening. The muscular fasciculi contained in this new tissue are sometimes normal in size, sometimes atrophied. The connective tissue is sometimes arranged in a regular manner round the muscular fasciculi, or it may be found in the form of plates or islets. This lesion is difficult to recognise with the naked eye, except in hardened specimens, which are divided and the surface stained with carmine: the sclerosed parts are then seen to be red. To justly appreciate this change the same parts of the heart, determined beforehand, must always be compared; thus, transverse sections of the *musculi papillares* of the left ventricle, from a series of healthy and diseased hearts, would give perfectly comparable results.

Tumours of the myocardium.—Gummata have been recognised in the cardiac muscle (Ricord, Virchow), and secondary nodules of carcinoma and epithelioma (Paget, Liouville). Recklinghausen has published a case of striated myoma in the heart of a new-born child. Thirty cases of hydatid cysts of the heart, almost always due to echinococci, have been recorded. These cysts may project into one of the cavities, for example into the right auricle, or they may rupture, or even become free without rupture.

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[1] Letulle, *Thèse de Doctorat*, 1880; Debove and Letulle, *Archiv. gén. de méd.* Mars 1880.

Normal histology of the endocardium.—The endocardium, which lines the whole internal surface of the heart, is composed of three layers: first, the endothelium formed of a single layer of flat cells; second, a layer of flat cells separated by a laminated ground substance; third, a layer formed of elastic tissue and connective-tissue fasciculi. The first of these layers generally disappears twenty-four hours after death, that is to say, at the time the autopsy is made. The lamellar layer is very thin on the ventricles, and on the two surfaces of the arterial and auriculo-ventricular valves; it is thicker on the auricles, and more so upon the left auricle than the right. The cells of this layer are thin, and have more or less numerous processes; they contain a lenticular nucleus, and are arranged parallel to one another, and are flattened towards the internal surface of the endocardium. The ground substance which separates them seems to be slightly fibrillated, or almost hyaline, so that at first sight the endocardium seems to be limited by an anhistic membrane. The thickness of this layer, measured in preparations obtained after dessication, soaked in carmine, and treated with acetic acid, varies from 6 μ to 10 μ. This layer, as well as the endothelium, is continuous without interruption, and passes from the superior to the inferior surface of the valves. The layer of connective and elastic tissue of the endocardium varies most according to the different regions of the heart; and sometimes so considerably that, for example, in the left auricle, where it is most developed, it is almost ten times thicker than in the ventricles. This layer is on one side directly continuous with the layer of flat cells, and on the other with the connective tissue which separates the muscular fasciculi. Fig. 234 represents at A a section of the ventricular endocardium, in which the layer of flat cells is seen at *a*, the fibro-elastic layer at *b*, and the connective tissue which unites these to the muscular fibres at *c*. It is composed of cells and elastic fibres; the latter are very delicate, and are arranged in layers parallel to the surface in the endocardium of the auricles; they are very numerous and pressed together: it is these fibres which give the surface of the left auricle the opaque, yellowish-grey appearance which it has normally. In the elastic layer of the ventricular endocardium the fibres are much less close.

In the auriculo-ventricular valves, the fibro-elastic layer of the auricle is continued upon the upper surface of the valves, becoming thinner; the fibro-elastic layer of the ventricular endocardium is continuous upon their under surface; it is much thinner than the preceding, and it gives origin to the tendons of the *musculi papillares*. The two elastic layers are separated from one another, in the substance of the valve, by a very thin layer of connective tissue. Hence, on section of the valve, at its free

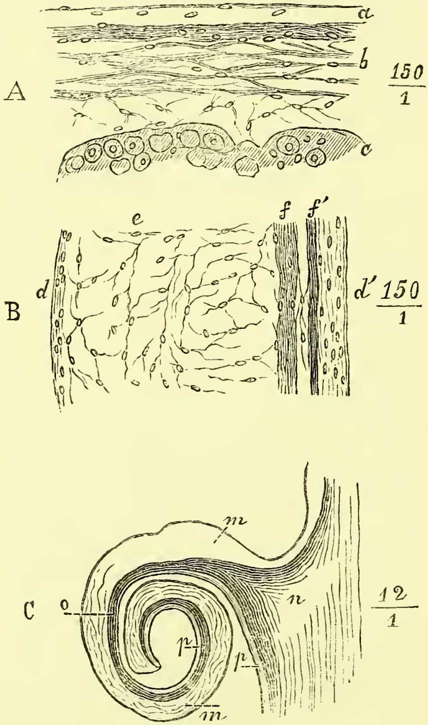

Fig. 234.—A, section of the ventricular endocardium: *a*, internal layer of flat cells; *b*, fibro-elastic layer; *c*, transverse section of muscular fibres. Magnified 150 diameters.
B, section of a sigmoid valve of the aorta: *d*, layer of flat cells on the superior surface of the valve; *d′*, the same layer on the inferior or ventricular surface; *e*, *f*, fibro-elastic layer of the aortic portion of the valve; *f′*, fibro-elastic layer of the ventricular portion of the valve.
C represents a section of an entire sigmoid valve with its insertion into the fibrous ring of the aorta: *n*, base of this ring; *m*, fibro-elastic portion derived from the aorta; *p*, fibro-elastic portion derived from the ventricular endocardium; *o*, elastic fibres. Magnified 12 diameters.

edge and both on its superior and inferior surfaces, may be distinguished the endothelium and the lamellar layer; then the two superior and inferior layers of the fibro-elastic tissue, the superior being the thicker, and finally at the centre a delicate layer of connective tissue. As we shall see later, it is always the superior or auricular surface of the auriculo-ventricular valves which is primarily altered, and also most extensively so in valvular endocarditis.

The arterial valves result from the union of the ventricular endocardium on the one side with the internal membrane of the artery upon the other (fig. 234, B and C). Beneath the epithelium is seen the lamellar layer (B, *d* and *d′*), which is continuous and reflected at the free border of the valves. This layer is thicker upon the ventricular surface *d′* than upon the arterial surface *d*. The fibro-elastic tissue, which separates the two united layers, is very thick at the origin of the valve (*c*, *m*). The internal arterial membrane forms four fifths of this thickness; thus on treating a section with acetic acid, which causes the thickened connective tissue of the upper surface to swell, it curls over, as is shown in fig. 234, C. We shall see later that valvular endocarditis is generally found on the internal surface, near the free border of the arterial valves, in the layer of flattened cells, which is thicker here than upon the external surface (B, *d′*).

Pathological Histology of the Endocardium.

Endocarditis.—Acute endocarditis occurs in acute articular rheumatism, puerperal fever, eruptive fevers, etc. The left ventricle is of all the cavities of the heart that in which it is most frequently met with, particularly on the aortic and mitral valves; and it is the auricular surface of the mitral and tricuspid valves and the ventricular surface of the aortic valves which are always primarily affected; that is to say, the surface of the valves which experiences the friction of the blood, in passing either from the auricles into the ventricles, or from the ventricles into the arteries. The old pathologists held redness to be of exaggerated importance in the anatomical diagnosis of endocarditis; but, if not seen in the form of vascular aborisation, this redness simply indicates imbibition, and is seen simultaneously upon the endocardium and upon the tunica interna of the blood-vessels. It is due to the impregnation of these membranes with the colouring matter of the blood, derived from the corpuscles which have been destroyed

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either by an infectious disease, such as pyæmia, variola, or by the rapid decomposition of the cadaver, as may be observed in hot and stormy weather.

Endocarditis is essentially characterised by vegetations, and by erosion and ulceration of the endocardium, which often lead to perforation and laceration of the valves. The **vegetations**, which constitute the essential phenomena of endocarditis, are often extremely small and numerous, so that they give to more or less extensive areas of the membrane a roughened or granular appearance: they may extend uniformly over a large surface of the auricle or the left ventricle. They are observed in this state at the commencement of endocarditis, but if the disease lasts some time they attain a larger size, which may equal that of a pea; they are extremely varied in shape, they may be conical, nummular, or raspberry-shaped, or even of the form of very long and delicate villi. Some groups of vegetations are very irregular, and are sometimes arranged on the borders of the sigmoid valves, or on the borders of the auricular surface of the mitral valve, near the insertion of the tendineæ, forming regular wreaths. Their situation is determined by the limit of the vascular network at the border of the valves. Thus, in the sigmoid valves they are not found on the sharp edge, but always at a little distance from it; this arrangement is particularly well marked in endocarditis which has been rapid and related to puerperal fever or acute articular rheumatism. The largest vegetations are only found on the valves or on the fibrous zone of the cardiac orifices. When the course of endocarditis is irregular and slow, the vegetations are very unequal in size. In the chronic forms they are less prominent, and rest upon an indurated base, and are hard, cartilaginous, and often opaque, while in the acute forms the recently formed vegetations are soft, friable, and semi-transparent.

The semi-transparency and brittleness of recent vegetations caused them to be long considered as composed solely of fibrin, though their adherence to the endocardium should have destroyed this hypothesis. On removing them with the nail, a loss of substance is seen in the membrane beneath, which shows very distinctly that the vegetation formed part of the membrane. This may be demonstrated by means of microscopical examination. After spreading the endocardium and the valves on a layer of cork, and submitting them to dessication, delicate vertical sections are cut, which, when stained with carmine, treated with acetic acid, and mounted in glycerine, show the following characters: in acute endocarditis the vegetations are formed entirely of embryonic tissue, which is continuous with the endocardium beneath and around the vegetations for a more or less extensive zone. This zone of proliferation should be studied with care, if the mode of formation of endocardial vegetations is to be understood. It will be observed that it is not sharply defined, but that from the healthy parts to the inflammatory foci there is a progressive multiplication of cells. The neoplasm is produced in the layer of flattened cells; the flat cells also concur, but it is nowhere shown that a certain number of cellular elements do not come from another source, for example by diapedesis of white corpuscles from the capillaries of the endocardium. The vegetations are covered with a hyaline layer formed of fibrin, which is more or less thick, though occasionally extremely thin; in covering the vegetations it may be prolonged in the form of delicate filaments, which may attain a great length.

In chronic endocarditis the vegetations have a different structure: the cellular elements, instead of being round, are elongated or flattened, they are separated by a fibrillar intercellular substance, always very abundant, and which gives them their cartilaginous consistence; the indurated plates on which they are implanted present a similar structure; in a word, the tissue which forms these vegetations and their bases recalls the structure of the internal layer of the endocardium. According to what is known regarding the course of all inflammatory products, it may be affirmed that all hard and prominent plates were originally soft vegetations, which have afterwards undergone fibrous organisation.

In the chordæ tendineæ of the mitral valves are observed the phenomena of acute or chronic endocarditis. In the first the chordæ soften though increased in size, and become so brittle that they may break at the moment that the valve acts. In chronic endocarditis hypertrophied chordæ tendineæ are frequently met with; they are diminished in length, are rigid, of cartilaginous consistence, and smooth upon their surface.

Instead of undergoing ultimate fibrous change, the soft vegetations of endocarditis may, under the influence of the shock of the blood, become easily torn off or into fragments, so that in their place are found irregularly torn shreds and loss of substance. The friable nature of these neoplasms results from the great number of cellular elements produced by acute inflammation. Exaggerated formation of cellular elements, coupled with insufficient nutrition, may sometimes cause their fatty degeneration, and the growing tissue of the neoplasm becomes disorganised, and an ulcerated anfractuous surface is then formed, in the borders of which are found granulo-fatty cells, free fat granules, and blood pigment. The portions which are torn, softened, and separated by the force of the blood-current are extremely small, and may be carried as far as the capillaries, or, if larger, they are arrested in the arterioles, producing septicæmia and embolism. This collection of symptoms has received the name of **ulcerative endocarditis,** but it does not constitute a distinct species apart from other forms of acute endocarditis. Some authors having, however, at the autopsy of persons who have died from ulcerative endocarditis, following puerperal fever for example, found bacteria in the base and edges of the fungoid ulcers of the endocardium, they have referred the septicæmic processes to these microscopical organisms. Klebs considers that the granular substance which covers the altered valves and the vegetations in ulcerative, rheumatic, or puerperal endocarditis is composed of a layer of micrococci.

Valvular aneurisms.—The lesion described under the name of valvular aneurism (Thurnam, Förster, Pelvet) is a consequence of acute endocarditis, located in the valves. Multiplication of the cells, their embryonic condition, softening of the intercellular substance, and disappearance of the elastic fibres, phenomena due to endocarditis, cause the valve to lose its power of resistance, so that it is unable to support the pressure of the blood. When, in acute endocarditis, all the layers of the valve rapidly undergo softening, it is first distended and may soon rupture; if the progress of the inflammation is, on the contrary, slow, the valve only becomes slightly less resistant, and is gradually distended without being ruptured.

Valvular aneurism has hitherto been only observed in the left heart, in the aortic and mitral valves. In the semi-lunar valves the orifice of the aneurism is always to be found on the superior or arterial surface; in the mitral valve it is always on the inferior or ventricular surface: this arrangement results from the direction of the blood pressure, which, the valves being shut, is from below upwards on the mitral valve during ventricular systole, and from above downwards on the semi-lunar valves during ventricular diastole.

At post-mortem examinations two forms of these aneurisms are found: first, a valve softened by inflammation may become distended throughout, and may remain in this state, which shows that, the inflammation having disappeared, the tissues of the valve have recovered their original firmness; second, the endocarditis continuing to be acute, one or more valves show ruptured aneurismal sacs upon parts of their surface; they are cup or funnel-shaped, and the holes in them are regular or torn; the edges of these rents are often formed of greyish, torn flakes, covered with a thin layer of fibrin, with projections towards the ventricle, on the sigmoid valves, and towards the auricle on the mitral valve. On examining these flakes by the method already indicated (section after dessication), nuclei and round cells are recognised, imbedded in a granular substance, and in the midst of this embryonic tissue neither fibrillar connective tissue nor elastic fibres can be found. The entire wall of the aneurismal sac is composed of the same tissue which is always met with in the substance of recent aneurismal sacs, whether intact or ruptured.

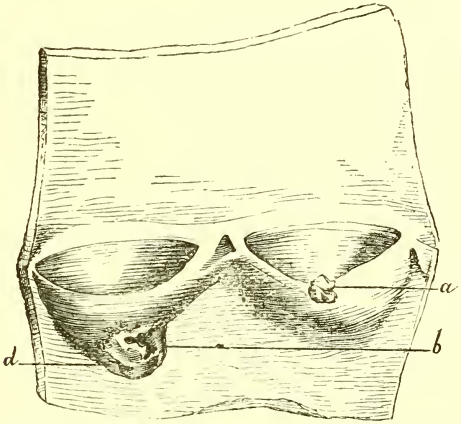

FIG. 235.—ANEURISM OF A SIGMOID VALVE OF THE AORTA.

The aneurismal sac, *d*, projects at the lower part of the valve; the orifice of the aneurism situated on its upper surface is not visible in the figure. In this case, the sac is already ruptured at *b*. *a*, vegetation in the adjoining valve.

Round or funnel-shaped valvular aneurisms are rarely seen without lacerations. When the sac has not been broken up into fragments by the blood pressure at the moment the valves close, there are more or less extensive rents, though these may be very small. We have, for example, seen an aneurism of a sigmoid valve of the aorta, in the form of a very long funnel, the extremity of which was simply perforated.

The vegetations and thickening of the endocardium produced by acute inflammation near the valves is a cause of stenosis of the orifices; but stenosis and incompetency are most frequently produced by simple chronic endocarditis.

Chronic endocarditis.—To chronic endocarditis is referred a series of cardiac lesions particularly found round the orifices; some of which are due to acute endocarditis which has become chronic, and others, of which the evolution is slow, are often observed in alcoholic subjects, in old age, and in lead-poisoning, etc. Chronic endocarditis is essentially characterised by semi-transparent or opaque cartilaginiform thickenings. In a great number of cases these nodules become infiltrated with calcareous salts and ossiform. Sometimes, however, these vegetations are formed of mucous tissue; they may acquire a considerable size, and even become united so as to form a single mass. M. Curtis has published a remarkable example of this (*Archives de physiologie*, 1874). It is particularly upon the fibrous zone of the orifices, in the chordæ tendineæ and valves, that the lesions of chronic endocarditis are usually observed. They have a strong resemblance to the lesions of endarteritis deformans, about to be described, and it is probable that in the endocardium, as in the arteries, primary atheroma plays a certain part.

The lesions of the valves in chronic endocarditis have the form of globular or wart-like vegetations, situated particularly on the ventricular surface of the sigmoid valves, and on the auricular surface of the auriculo-ventricular valves. The chordæ tendineæ of the auriculo-ventricular valves are thicker, shorter, and indurated; the fibrous zone of the orifices is hypertrophied and indurated. When the heart is dilated in consequence of the blood pressure, the fibrous rings of the orifices often undergo similar dilatation. At other times, on the contrary, these rings are thickened and show marked contraction. The valves themselves are two, three, or four times their normal thickness, their tissue is rigid, and their edges are roughened and irregularly thickened; equally thickened at their origin, the fibrous zone, to which they are attached, shows similar induration. It hence results that the general shape of the orifices is greatly changed. Incompetency and contraction may exist at the same time—incompetency from rigidity of the valves, and contraction from new growths on their edges: it is, in fact, rare for contraction not to be complicated by incompetency.

Microscopical sections of the indurated tissues show profound changes in the structure of the endocardium. Instead of finding the successive layers which have been described, and which are so characteristic of each part of the valves and orifices, only irregular collections of flat cells are found, separated by a fibrous substance or irregularly distributed elastic fibres. Cellular development has produced this disorganisation of the tissues, and has been the point of departure of a new organisation, which tends to reproduce the primitive structure, without ever completely succeeding. In this imperfect fibrous tissue, centres of fatty degeneration are constantly found, which, on becoming united, form atheromatous foci filled with granular detritus. These foci remain stationary or open on to the surface. The formation of calcareous plates and granules, or true petrifactions, are very often observed in the indurated tissues of chronic endocarditis. At the commencement of this disease the new formation of cells takes place in the layer of flat cells; when, in consequence of this development, new fibrous layers are produced, they evidently tend towards cicatricial contraction. Hitherto, however, this process has not been followed under the microscope.

The formation of blood clots in the heart.—At the autopsy the left ventricle is most frequently found collapsed and emptied of blood, except a few filamentous clots between the columnæ carneæ of the mitral valve; it is only in the case in which death has been caused by syncope that the ventricle, arrested in diastole at the moment of death, contains fluid blood and clots. The right ventricle is frequently distended and filled with coagulated blood: this phenomenon must be attributed to the fact that during the death agony asphyxia and hindrance to the pulmonary circulation prevent the right ventricle from emptying itself. The auricles, owing to the feebleness of their contraction, always contain blood during life, and are consequently always filled with blood after death.

When the heart ceases to beat, the blood contained in its cavities slowly coagulates, much more slowly than if it were contained in a vase: this fact was established by the experiments of Brücke, who observed that blood retained in the cavities of a heart removed from the animal did not coagulate for some hours, and he attributed this phenomenon to the influence of the endothelium of the endocardium. Now it is known, on the other hand, that whenever the blood coagulates slowly the red corpuscles fall to the bottom, while the superficial part, deprived of corpuscles, coagulates into a colourless fibrinous mass. The clot is then composed of two layers, one superficial, composed of fibrin with serum entangled in its meshes (the buffy coat of inflammation), and the deeper layer strongly coloured red by the red corpuscles. This is the mode of coagulation observed in the heart when there is a large quantity of blood in its cavities, and the body, for some hours preceding the autopsy, has lain, as is usual, on the back. All the large clots of blood are decolorised on their anterior superior surface, while they are cruoric on their posterior inferior surface. Most physicians who perform autopsies consider that these clots are formed during the death agony; on account of their decolorisation, they assign them a vital origin, and call them active clots. What we have already said regarding the formation of clots is sufficient to show that this interpretation is erroneous, and it is useless for us to insist upon it further.

Some clots may be called **active clots**, if by this name it is understood that they are formed during life: these are the fibrinous concretions developed in delicate layers, upon the denuded surface of the endocardium, in endocarditis, or upon vegetations of the orifices or ruptured valves. These clots are white or yellowish; they do not contain red blood corpuscles, but are solely composed of laminæ of granular fibrin. According to the theory of A. Schmidt, which is generally accepted, their formation is the result of the coagulation of the fibrinogenic substance of the blood in contact with the inflamed wall. This explains why this coagulum, which is formed slowly, does not contain the figurate elements of the blood.

Other larger clots are formed in consequence of the slowing of the blood current, as may be observed in asystole of pulmonary origin, and in hypertrophy of the heart with dilatation. These clots are very variable in form and size; they are wedged in between the columnæ carneæ, and are adherent to the walls of the heart; they are uniformly yellowish, and when not very old they may be separated into laminæ by tearing, showing that at the centre they are as firm as at the periphery. When older, they are firm superficially, while their centre is softened, and forms a granular detritus in which white corpuscles may always be found, sometimes in very considerable numbers.

When the blood is profoundly altered, as in hæmorrhagic variola, puerperal fever, phosphorus-poisoning, etc., the clots formed in the heart after death are soft, friable, and are not composed of distinct layers. In leukæmia the clots are quite colourless, and beside them is found a fluid which has often the appearance and consistence of pus, as Virchow observed: this is due to the enormous quantity of white corpuscles contained in the fluid.

CHAPTER IX.

LESIONS OF THE ARTERIES.

I. Normal Histology of the Arteries.

The arteries present for study internal, middle, and external coats. The internal coat of the large arteries is composed of two layers: first, an epithelial layer; second, a delicate layer, from ·003 mm. to ·012 mm. in thickness, lying upon the middle layer. The **epithelial layer** is formed of a single row of soft polygonal cells, elongated in the direction of the vessel, and much flattened; in preparations stained with nitrate of silver they are seen by transmitted light to be bordered by a black line; each cell contains a flat, circular, or elongated nucleus, which may be made evident by staining with picro-carminate of ammonia. The **sub-epithelial layer** is formed of flat, irregularly stellate cells, anastomosing together, and containing flat nuclei; they are imbedded in a ground substance, which is fibrillated in a longitudinal direction. In the small arteries this layer is extremely thin, while in the aorta it is relatively thick, and composed of two fibrillated layers, in the most internal of which the fibres have a longitudinal direction, while they are transverse in the external layer. The **middle coat** is, in the aorta and carotid, composed of elastic laminæ and fibres which form by their anastomoses a continuous system, and limit lacunæ in which are contained smooth muscle cells lying in a transverse direction, and a few connective-tissue fibres. Next the internal coat, the middle coat is bordered by an elastic layer, thicker than the others, and which is seen to have a festooned appearance in transverse sections. The recognition of this elastic layer is very important in the pathological histology of the arteries, and we have therefore named it **the internal elastic layer of the middle coat.** On the side of the external coat, the elastic fibres are detached from the elastic laminæ of the middle coat, and are distributed between the fasciculi of connective tissue in various directions, and thus constitute the framework of the external or adventitious coat.

In the femoral, brachial, and all arteries of a medium calibre, the middle coat has only one elastic layer, which is the internal elastic layer. The transverse muscle cells form flattened fasciculi, separated from one another by connective tissue and elastic fibres, continuous with the internal elastic layer on one hand, and on the other with the large-meshed elastic network of the external coat. The internal and middle layers have no blood-vessels, the external coat is, on the contrary, supplied with arteries, capillaries, and veins, and with lymphatics whose lumina are seen as clefts in transverse section; small nerve trunks and isolated nerve tubes are also present. The small arteries have a middle coat formed of smooth muscle cells arranged transversely side by side, so as to form a continuous membrane. The adventitious or external coat is composed of small fasciculi of connective tissue, having in general longitudinal direction.

II. Pathological Histology of the Arteries.

Arteritis.—The inflammatory lesions of the arteries are many and various. Inflammation of the arteries may be considered according to its seat in the large, middle, and small arteries, or in the internal, middle, and external coats. Atheromatous and calcareous degeneration should also be studied with arteritis; finally, spontaneous aneurism and the histological changes which occur in arteries obliterated by a blood clot also belong to arteritis. We shall therefore describe successively, first, acute arteritis; second, chronic arteritis and atheroma, so frequently combined; third, aneurisms; fourth, arterial obliteration. In this description we do not propose to divide inflammation of the arteries, with reference to its seat in the tunica interna (endarteritis) or in the tunica externa (periarteritis), for endarteritis and periarteritis are most frequently combined: we shall, however, carefully indicate the cases in which these two lesions are seen separate.

Acute arteritis.—Acute endarteritis, or acute inflammation of the tunica interna, is often seen in the aorta as an isolated lesion. It is characterised by swelling of the tunica interna in the form of prominent patches, more or less extensive, the contour of which is irregular or circular: some of these patches are small, regular, and acuminated; others, more extensive and irregular in outline, are evidently formed by the confluence of many similar round patches, and show prominences and depressions on their surface. They are generally pink, transparent, or more or less opalescent, and are elastic, soft, and gelatinous in consistence—thus they are generally known by the name of 'gelatinous patches of the aorta'; their surface is very rarely ulcerated. Round them the tunica interna is not entirely healthy; it is tumefied and slightly softer, appearing as if it had imbibed fluid; it is sometimes pink, at others colourless. In some cases, in which the endarteritis is very intense, we have been struck with the pallor of the tunica interna, while, on the other hand, we have frequently seen the vessels and endocardium of a deep red, due solely to imbibition without there being any trace of endarteritis or endocarditis. It is, however, sufficient to macerate an artery in blood-stained water for its surface, which was originally pale, to become reddened by infiltration of the hæmoglobin dissolved in the water. In subacute and less chronic forms of endarteritis the free surface of the artery is shagreened and deprived of its polish, which is due to the irregular tumefaction of the tunica interna of the vessel.[1]

The gelatinous patches of acute endarteritis seem, in vertical sections, to be composed of the same transparent tissue which limits the middle coat of the artery. On removing one of these gelatinous patches, and dissociating it with needles, its constituent elements are isolated without difficulty. They are, first, spherical or irregularly spherical cells, of a mean diameter of ·01 mm., and in which a nucleus is seen after the addition of acetic acid; they have, in fact, the characters of embryonic cells. Secondly, a few large flattened cells, with multiple processes, containing sometimes two nuclei, and corresponding to the normal connective-tissue cells of the internal membrane. The round elements, obtained by dissociation, are cells and not simply nuclei, as might be thought on examining them merely in sections obtained after dessication, which is the process usually employed. In such sections the patches appear as a thickening of the tunica interna. With a low power, the considerable thickness of these patches compared with normal parts of the internal membrane, and even with the middle coat, may be appreciated; they may be a hundred times thicker than the normal internal coat, and two or three times thicker than the middle coat. With a power magnifying a hundred diameters, which allows of the whole preparation being seen, it will be observed that the cellular elements are extremely numerous, arranged close together in lines parallel to the surface, their number diminishing progressively, as the deep layers near the middle coat are approached. We cannot avoid seeing in this phenomenon a striking analogy with that which takes place in inflamed diarthrodal cartilages, in which the cells on the surface are also the first to multiply.

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[1] This roughened and unpolished appearance of the internal membrane in endarteritis has been often referred to exfoliation of the epithelium. We may here remark that exfoliation of the epithelium cannot be the cause of this appearance, for twenty-four hours after death the epithelium has disappeared, from the smooth as well as from the roughened surfaces, both in normal and pathological conditions.

The fact of the multiplication of elements on the surface of the internal membrane is peculiar to acute endarteritis, and separates it from endarteritis consecutive to atheroma, in which proliferation occurs, as we shall see, in the deep layer of the internal membrane. The same distinction may be made in endocarditis.

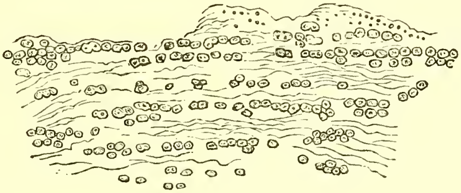

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Fig. 236.—Section of the Tunica Interna of the Aorta, in a case of Acute Endarteritis.

This section, made after dessication of the artery, shows the proliferation of the elements of the internal membrane. Magnified 200 diameters.

At the periphery of the gelatinous patches where continuous with the tunica interna, a series of modifications of this membrane may be observed, and the process of their formation and development followed. Near the tumefied parts there is also in the tunica interna a large number of round cellular elements, while deeper are still found flattened cells with lenticular nuclei. With a higher power, and in preparations treated with acetic or formic acid, the substance of the cell cannot generally be seen round the nuclei, which seem to be simply imbedded in a ground substance. This, as we have already pointed out, is an optical illusion, due to the method of preparation. Upon the surface of the gelatinous patches the cellular elements are so close together that many of them seem to touch: nuclei may here be seen biscuit or hour-glass-shaped, which indicate that division is about to occur, and also groups of from two to five nuclei in contact with one another (*vide* fig. 236). In the deep layers the ground substance is more abundant, and the groups of cells more separated.

The presence of numerous cellular elements in the superficial layers of the tunica interna cannot be explained by diapedesis, since this membrane does not contain blood-vessels. Migration through the internal coat of white corpuscles derived from the blood circulating in the diseased artery is the utmost that can be allowed. But it is much more probable that they are derived from cells normally present in the tunica interna, and these cells moreover show in the clearest manner signs of division of their nuclei (*vide* fig. 236).

The gelatinous patches of arteries sometimes show superficial and fungoid ulcerations, which are covered by a thin layer of adherent fibrin. This soft, semi-transparent layer often shows red spots or lines, and sometimes it is stained throughout its whole extent. It cannot be determined, without examining microscopical sections, whether this layer be fibrin or the modified internal membrane. The elements composing this transparent layer, when studied by dissociation, are easily isolated, and are seen to be numerous, round, small uni-nucleated cells. It cannot be determined by their form alone whether these cells are embryonic elements such as we have described in the proliferating tunica interna, or white blood corpuscles; but in vertical sections, cut after hardening in alcohol, fibrin may be recognised, including cellular elements. It is probable that the fibrinogen of the blood is transformed into fibrin by the presence of the fibrinoplastic substance of the inflamed parts, and that the elements entangled in its network are either white blood corpuscles, or the free and proliferating elements of the diseased surface.

The **middle coat** does not usually present any alterations in acute endarteritis.

Between the most acute endarteritis and the chronic form at its final stage, all intermediate forms may be found ; it may even happen that all the phases may be met with in the same segment of an artery.

Periarteritis.—In almost every case of acute endarteritis, periarteritis is present, that is to say, an inflammatory thickening of the tunica externa. The tissue of this coat becomes homogeneous, gelatinous, and of an amber or pink colour. Microscopical sections show marked thickening and a new formation of cells between the fasciculi of connective tissue. Acute periarteritis, characterised by purulent inflammation of the tunica externa, is seen in phlegmon; the inflammation is most frequently limited to this membrane, or a slight lesion of the tunica interna may be present; in all cases the middle coat is not modified in a marked manner. The resistance of the arterial walls is preserved, neither distension nor laceration occurring, and the function of the artery is not interfered with.

Acute inflammation of arteries of middle and small calibre is rarely primary, but is frequently seen in consequence of inflammation of neighbouring tissues. Thus in the lips of a granulating wound, in the fungoid tissue of whitlow, in the base of a chronic ulcer, the small divided arteries will, on section, be seen, with the unaided eye, as minute red spots surrounded by a semi-transparent, thick, circular zone. On attempting to dissect out the arteries, it will be found difficult to trace them far, for their external coat, infiltrated with inflammatory fluids and elements, is blended with the neighbouring connective tissue, and forms with it a single lardaceous mass. In this dissection also it will be found that the vessels are brittle, and slight traction in the process is sufficient to tear them. Arteries thus thickened by inflammation are difficult to distinguish, with the naked eye, from neighbouring nerve cords.

Histological examination of diseased blood-vessel is made in sections carried through its various coats and surrounding tissues, after hardening. Vegetations of the internal coat, that is to say, of the part comprised between the internal surface of the blood-vessel and the internal elastic layer, will be then observed. In these growths, which vary in form and extent, are seen round cells, or cells flattened in different planes, separated from one another by a small quantity of intercellular substance. Blood-vessels from the tunica adventitia penetrate and form loops: this vascularisation is observed when the middle coat has disappeared, or has been transformed into connective tissue. As to the external coat, its connective-tissue fasciculi and elastic fibres are kept apart by a more or less considerable number of embryonic cells, which may determine, as in all inflammation of the connective tissue, absorption of the connective-tissue and elastic fibres. The middle coat is, as we have already seen, not always left intact; in it may be observed multiplication of cells, which cells are undergoing differentiation from the muscular type, and are absorbed at the same time that the elastic fibres break up. Finally, the different arterial coats are blended together for more or less extensive areas. Under the influence of inflammation the various tissues constituting the arterial walls tend to take the structure of the inflamed tunica interna. When considering aneurisms, we shall see some remarkable examples of the transformation of the external and middle coats into a tissue resembling that of the internal membrane.

When vegetation of the internal coat is so considerable as to impede or arrest the course of the blood, it coagulates above the growth: this is one of the forms of arterial thrombosis.

Chronic arteritis.—The lesions of chronic arteritis are similar to those of acute arteritis, only that they are complicated with fatty degeneration, calcareous change, and atheroma. Calcareous change is always accompanied with arteritis, which is not always the case in fatty degeneration, which may be alone, and which we consider to be one of the causes of arteritis. Thus we shall commence by studying primary fatty change of the arteries.

Primary fatty degeneration of the arteries is seen principally in the aorta, immediately above the sigmoid valves, where, in almost all adult persons, will be found whitish, opaque spots, forming a hardly perceptible elevation. These spots may be considered as the first stage in fatty degeneration with atheroma and calcareous

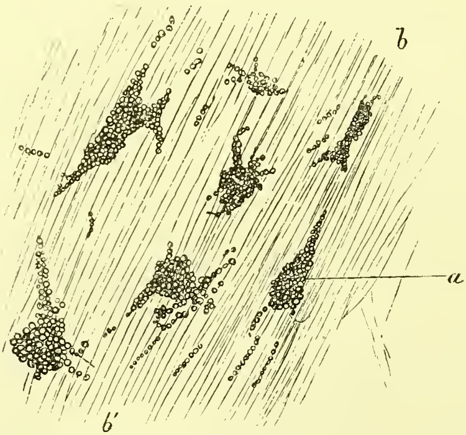


Fig. 237.—Fatty Degeneration of the Tunica Interna, in a Flake of this Membrane.

In the midst of the fibrillated tissue, *b*, are seen masses of fat granules resulting from the fatty degeneration of the flat ramifying cells of this layer. Magnified 200 diameters.

plates, which, in persons more advanced in age, may be of considerable extent. These white or yellowish patches may be examined in longitudinal sections, prepared according to the method already indicated (p. 492). They may also be examined in flakes detached from the tunica externa and extended on a slide. In these flakes are observed collections of granules and drops of fat, which frequently have the shape of the flat ramifying cells of the tunica interna (fig. 237). In vertical sections, it may be seen that the fatty degeneration is not limited to the tunica interna. The internal layers of the tunica media are also affected in the same manner.

In the tunica interna the fat granules form flattened or fusiform collections, in the midst of which nuclei may sometimes be distinguished; they are recognised by being stained red, when the preparation has been submitted to the action of carmine, while the fat granules are not coloured by the same reagent. Most of the collections, however, do not contain nuclei, these having atrophied and disappeared.

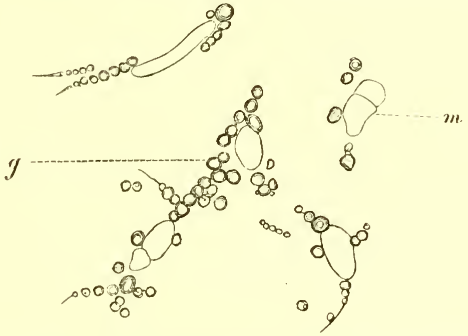


Fig. 238.—Fatty Degeneration of the Tunica Interna of the Aorta.

m, nuclei of the flat cells; *g*, fat granules. Magnified 400 diameters.

In the tunica media the fat granules are deposited between the elastic fibres and laminæ, and, when very profuse, the muscular elements are no longer distinguishable. At the edges of the parts which have undergone fatty degeneration the muscle cells are infiltrated with fat granules.

It may be concluded from these data that fatty degeneration causes atrophy of the affected elements; that there is, in the full acceptation of the term, a fatty necrobiosis.

Chronic endarteritis.—When a portion of the arterial coats has undergone the fatty degeneration just described, it becomes necrosed, and determines around itself the phenomena of irritation. Chronic endarteritis is thus produced ; but this is not the sole cause of chronic endarteritis : it may be produced spontaneously, or succeed rheumatic, puerperal, or alcoholic endarteritis. The lesions of chronic endarteritis, whatever may be its origin, are always complicated by fatty degeneration of the arterial coats, leading to the formation of atheromatous foci and calcareous plates. An analysis, as complete as possible, of all these phenomena ought to be made before determining their order of succession. Fatty degeneration may, indeed, be the cause or the result of arteritis. In subacute arteritis the gelatinous patches may contain stellate cells in a state of fatty degeneration ; but this process of degeneration continuing when the inflammation has lost its first intensity, almost all the cellular elements of these patches become charged with fat granules, and thus lose their semi-transparency to become yellow and opaque. These groups of granules, which have the form of stellate cells, soon become fused together, and form small foci, which can at first only be recognised under the microscope, but which later on increase in size, and appear to the unaided eye like atheromatous foci.

The atheromatous foci are situated in the thickened tunica interna. They are large and shallow, with anfractuous borders. They are at first separated from the blood current by a delicate cartilaginiform pellicle, composed of the most superficial layers of the internal coat ; this pellicle is tense though mobile ; at its periphery is often observed a cord-like swelling, formed by a thickening of the tunica interna, so that the centre of a non-ulcerated atheromatous patch is slightly depressed.

On making a vertical incision through the centre of the atheromatous patch, the scalpel, after being momentarily arrested by the hard superficial layer of the tunica interna, opens a focus, out of which escapes a thick whitish fluid, which, examined under the microscope, is seen to contain a large quantity of cholesterin, free fat granules, granular bodies, and crystals of fatty acids.

Atheromatous foci open rather frequently during life into the artery, in consequence of the progressive thinning of the pellicle covering them, or from the friction and shock of the blood current against the vascular wall ; the opening is generally effected by a small slit or star-shaped rent. The contained detritus then passes into the circulation, and the blood penetrates the focus, the contents of which take a yellow, brown, or black stain, due to the transformation of the hæmaglobin. Such foci may be the point of departure of small cup-shaped or crateriform aneurisms, which will be considered later.

In microscopical section passing vertically through the atheromatous focus and its borders, it may be seen that its basis is composed of the deeper layers of the tunica interna, which shows the lesions of endarteritis with fatty degeneration. The most superficial layer of the tunica media also shows signs of primary fatty degeneration. On the borders of the patch of atheroma the swollen parts show microscopical atheromatous spots situated in a slightly fibrillated substance ; more distant from the focus are found nuclei of cells which stain with carmine, and are surrounded with fat granules; still further, the fibrillated substance limits small cavities or lacunæ containing cells resembling those of cartilage, but which are not surrounded by capsules. This is a chondroid, but not cartilaginous, change of the tunica interna. When the evolution of atheroma is slow, the fibrillated ground substance becomes infiltrated with calcareous granules, at the same time that the cells undergo fatty degeneration. These granules, solitary at first, afterwards unite so as to form imbricated semi-transparent, brittle, and inelastic plates.

Calcareous plates.—It is rare for calcareous plates to be completely exposed on the surface of a vessel; they are generally covered by a layer of the tunica interna. These plates, which are often extremely thin, are broken by the shock of the blood current, or their edges are raised, tearing the delicate layer of tissue which covers them, so that fenestræ are made, through which the blood insinuates itself beneath the plates, marking its track by black pigment. The before-mentioned properties of transparency, brittleness, and inelasticity, which these calcareous plates possess, distinguish them at once from osseous tissue, which is, on the contrary, resistant, opaque, and elastic. On making preparations of them by the methods described for the study of bone (*vide* p. 326, note), the structure of osseous tissue is never found; they only show irregular masses, black slits and striæ, in the midst of a very transparent substance, which shows neither the laminated arrangement nor the blood-vessels of bone. These slits and striæ have no resemblance to bone corpuscles.

Arteritis deformans.—In old age all the lesions already described are often seen accompanied with dilatation of the vessel; to this complicated pathological condition the name of arteritis deformans has been given. On removing and opening an aorta affected with this disease, the increase of its diameter, the inequality of its calibre, the irregularity of its surface, and the variety of the lesions present are very striking. These lesions are generally more pronounced and older at the origin of the aorta than in the rest of its course; they are, however, continued into its branches; it seems as if the alteration commenced at the origin of the aorta, progressively invading the rest of the arteries. Above the sigmoid valves, which are generally indurated, are seen calcareous plates, separated by slits or imbricated, and bounded on their borders by the swollen tissues of endarteritis. These calcareous plates most frequently extend into the coronary, innominate, carotid, and subclavian arteries, invading them for a more or less considerable extent. At their point of origin in the aorta these arteries generally show almost complete ossiform rings. The arch of the aorta is usually dilated, from which it results that the thoracic aorta has the form of an elongated funnel. Beside the calcareous plates may be seen open atheromatous foci, atheromatous pustules, and cartilaginiform plates. The extent and thickness of the latter are variable; they are semi-transparent or more or less opaque, and are often accompanied with nummular excrescences or vegetations covered with layers of fibrin varying in thickness. It frequently happens that the thin, vitreous, calcareous plates, formed in the hypertrophied and rigid internal membrane, or extended over atheromatous foci, crack, and the blood infiltrates through the narrow slit. The blood undergoes the usual pigmentary changes, and forms black or melanotic patches of various extent, giving the diseased part an altogether peculiar appearance.

The preceding description applies particularly to the aorta; but the same lesions are observed in arteries of medium and small calibre, in which calcareous degeneration, so frequent in old persons in the arteries of the limbs and brain, originates in the hypertrophied tunica interna by chronic endarteritis. This endarteritis is histologically characterised by multiplication of the cells of the tunica interna, and by the formation of a resistant and slightly fibrillated intercellular substance, which soon gives a cartilaginous consistence to the membrane. This chondroid tissue may be developed regularly in the tunica interna so as to diminish the calibre of the vessel in every direction; or its development may be exaggerated in certain spots, thus forming plates or buds projecting into the lumen of the vessel. In consequence of this lesion the blood current is slowed in the affected arteries so that coagulation may take place This arterial thrombosis produces gangrene in the extremities, softening in the brain, and fatty degeneration of the heart when located in one of the coronary arteries.

Chronic periarteritis.—All forms of arteritis of long standing are accompanied with thickening of the tunica externa, and the production of numerous cells between the fasciculi of the connective tissue; in a word, it is complicated with chronic periarteritis. In dilatation of the aorta accompanying arteritis deformans, it constantly happens that the middle coat disappears at certain points, and the hypertrophied internal coat becomes united to the external. The destroyed portions of the middle coat are replaced by proliferating connective tissue of the external and internal coats. Fig. 239 shows an interruption of this nature of the tunica media of the aorta; it is seen as a bridge thrown across the solution of continuity between the internal and external coats. The blood-vessels, often contained in these bridges of fibrous tissue, reach the tunica interna and ramify, thus showing how it is that this membrane may become vascular. The destruction of the tunica media is the immediate cause of spontaneous aneurisms of the aorta.

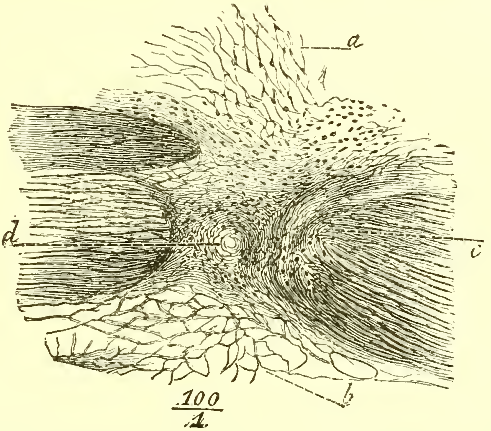


Fig. 239.—Section of the Aorta at a Point where the Middle Coat is interrupted by Connective Tissue.

a, tunica interna; *b*, tunica externa; *c*, tunica media; *d*, blood-vessel in the midst of embryonic tissue, which unites the external and internal membrane. Magnified 100 diameters.

Before the disappearance of the middle coat, in consequence of endarteritis and periarteritis, its elastic laminæ and fibres are decomposed into small and refractile granules. The external coat is itself so modified in structure that it takes the histological characters of the internal coat, and is seen to be formed of flat cells, parallel to the axis of the vessel, separated by a slightly fibrillated ground substance. This change which it undergoes in structure may be due to the pressure exercised by the blood current on its irritated connective tissue, which is no longer protected by the elastic and resistant elements of the middle coat. These interesting modifications may be seen in the development of all spontaneous aneurisms.

Aneurisms.—Authors have divided aneurisms according to the form of the aneurismal sac into *cylindrical*, *fusiform*, *sacculated*, *crateriform*, or *cup-shaped*. They have also been classified according to the notion formed of the structure of the wall of the aneurismal sac, into *true aneurism*, formed by the dilatation of the three coats of the artery, *mixed external aneurism*, formed by the external coat, the two others having disappeared, and *mixed internal aneurism*, in which the sac is composed of the internal coat alone, and forms a hernia between the two torn or separated external coats. *False aneurisms* are those in which the aneurismal sac is solely composed of the neighbouring tissues of the blood-vessel, after rupture of its walls, and finally *dissecting aneurisms* in which, the internal and middle coats having ruptured, the blood infiltrates between the external and middle coats, separating them for a certain distance.

The anatomical data on which authors have based this classification are, for the most part, entirely false, as we have shown in a former work. Their errors arose from considering that aneurisms were formed as the result of simple mechanical action exerted upon a healthy artery, while the fact is that spontaneous aneurisms are always developed in arteries which have been for a long time the seat of inflammatory lesions. We have already seen that in the case of the simplest aneurism—dilatation of the aorta in arteritis deformans—the internal and external coats undergo profound changes and become hypertrophied, while the middle coat partially disappears; from which it results that this aneurism, considered hitherto as a true aneurism, is not true, since the middle coat is wanting in places: it is neither a mixed external nor a mixed internal aneurism, since the two internal and external coats are well preserved, although modified in structure. It is the same with all spontaneous aneurisms. Thus the anatomical classification of authors ought to be absolutely rejected. We consider that all spontaneous aneurisms are identical from the histological point of view, that is to say, that their sac is formed by the internal and external coats, modified by inflammation, and dilated by the blood pressure, the middle coat having totally or partially disappeared.

Fusiform aneurisms are produced by the circumscribed dilatation of an artery, a limited portion of which becomes regularly distended throughout its whole extent. This lesion is related to arteritis, which affects regularly the whole segment of the vessel.

Sacculated aneurism is produced when the inflammation affects only one side of the artery, or there attains its maximum; the middle coat being here destroyed, dilatation occurs solely at this spot.

Cystogenic or cup-shaped aneurisms are small and communicate with the artery by a circular aperture with sharp edges; the sac is regularly hemispherical; they are generally found at the origin of the aorta, and appear to be formed by atheromatous foci which have opened and become distended.

Dissecting aneurisms, first described by Laennec, owe their formation to a sudden accident occurring in an artery modified by chronic inflammation. Laennec supposed that after rupture of the internal and middle coats the blood insinuated itself between the middle and external coats dissecting them; but Peacock has shown that the blood is diffused either between the hypertrophied internal coat and middle coat, or between the layers of the middle coat itself. The external coat, being normally composed of connective-tissue fasciculi which glide over one another, would be incapable of holding blood submitted to arterial pressure. Many authors, MM. Ball and Duguet among others, have completely verified the observations of the English author.

Stratified clots.—Every circumscribed aneurism, whether sacculated, fusiform, or cup-shaped, presents for consideration the membrane or wall of the sac, and the stratified clots which line its internal surface. On opening an aneurismal sac, there are found in it fluid blood, soft clots of recent formation, greyish, semi-transparent laminæ of elastic fibrin showing opaque striæ, and which are easily separated. The last of these laminæ may also be detached from the internal surface of the sac. It often happens, principally in large aneurisms of the aorta, that the most external of these fibrinous laminæ, that is to say, those which touch the wall of the aneurismal sac, have undergone granular degeneration; they first become opaque, and then break down, forming irregularly shaped cavities filled with an atheromatous detritus. The walls of these cavities show fibrinous lamellæ cut as if with a punch in an irregular manner, the arrangement calling to mind the stratification of chalky ground, cut perpendicularly by a landslip or by the hand of man.

The arrangement of these layers of fibrin in the interior of the aneurismal sac is variable. In the simplest cases, principally in cup-shaped aneurisms, the layers of fibrin form superimposed strata, of which only the most external are at the bottom of the sac; the subsequent layers are consequently more extensive, and only the most internal reach the neck of the sac. These layers consequently vary in extent, the smallest being most external, and the largest most internal. This arrangement marks the progressive growth of an aneurism. The oldest, that is, the most external clots, were formed when the sac was still small, and they remain of the size that they then had; the other clots were deposited while the sac was increasing in size. In large aneurisms, the arrangement of the stratified clots is not so simple; but the changes which have been produced suddenly are still capable of recognition; for example, in one part of an aneurismal sac may be observed superimposed fibrinous laminæ, forming by their union the segment of a sphere, the diameter of which is less than that of the aneurismal sac; these may be compared to the collection of fibrinous clots described in sacculated aneurism. Upon these laminæ, which were evidently the first formed, are obliquely deposited the new layers, forming segments of a much larger sphere; these laminæ may extend from the internal surface of the sac to terminate at its neck. According to the structure of aneurismal sacs, it is evident that a sacculated aneurism, originally small and lined with layers of old fibrin, is, at a given moment, suddenly distended; the enlarged cavity of the sac then becomes lined with more extensive layers of fibrin. Still more complicated arrangements are sometimes met with, which are easily understood and explained by the more or less sudden enlargement of the aneurismal sac at different periods in its evolution.

The laminæ of fibrin are the more resistant and delicate the more external they are. In thin sections fibrils of recently coagulated fibrin are not found, but irregular laminæ, between which are seen collections of fat granules and blood pigment; these collections form the opaque striæ spoken of above; lacunæ which seem to be canaliculated (Vulpian) may be also perceived; but in these clots no true organisation resembling a tissue can be seen. Neither living cells nor blood-vessels are observed, only, after the action of carmine and acetic acid, corpuscles stained red are seen ; they are vestiges of the white corpuscles imprisoned in the fibrinous coagulum. In the atheromatous detritus, which is sometimes substituted for the laminæ in contact with the wall of the sac, are found proteid and fatty granules, crystals of cholesterin, and caseous white blood corpuscles.

The aneurismal wall.—In order to examine the aneurismal sac flakes are removed and dried, and sections cut, which are softened in water, stained with carmine, and mounted in glycerine to which formic acid has been added. In some of these preparations the membrane composing the aneurismal sac seems to be formed of a single tissue, the structure of which resembles that of the internal coat of the aorta modified by inflammation ; in other preparations the middle coat is found very much thinned (*b*, *b*, fig. 240), and beyond it the external coat, which has become similar to the internal. There are often only a few irregular vestiges of the middle coat left, imbedded in a tissue, which recalls the characters of the internal coat of large arteries affected with chronic endarteritis. By attentive examination of different regions of the same aneurismal sac, it may be recognised that the middle coat has completely disappeared round the centre of a fusiform, and at the bottom of a sacculated aneurism ; irregular patches are, however, constantly met with as the non-dilated portion of the artery is approached. Near the neck of the sac the thinned middle coat is continuous, or interrupted only by a few bridges of vascularised tissue, interposed between the external and internal coats.

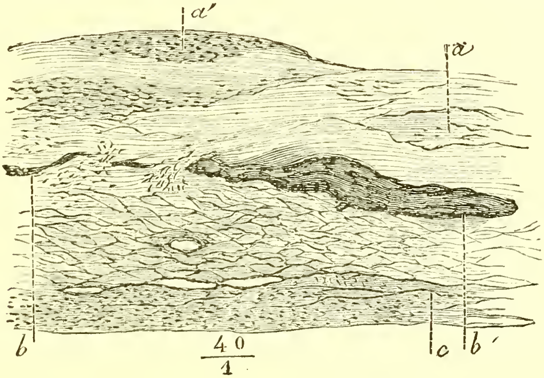


FIG. 240.—SECTION OF THE WALL OF AN ANEURISM OF THE AORTA.

a, tunica interna, showing at *a'* a prominent plate ; *b*, *b*, vestiges of the tunica media ; *c*, tunica externa. Magnified 40 diameters.

The newly formed tissue, which partially or entirely constitutes the sac of the aneurism, is composed of collections of flat cells separated by a slightly fibrillated substance; it undergoes the same modifications as those observed in chronic endarteritis, that is to say, fatty degeneration, atheroma, and petrifaction; old aneurismal sacs may be met with formed of a solid inextensible calcareous shell.

The lesions of chronic endarteritis and the structure of aneurismal sacs being understood, it is easily comprehended how aneurisms develop and enlarge. Of all the coats of the arteries, the middle coat is the only one which is able, by reason of its elastic contractile elements, to effectually resist the pressure of the blood wave. When, in consequence of endarteritis and periarteritis combined, the middle coat has disappeared from fatty degeneration of its muscular fibres, or from the granular breaking down of its elastic fibres, the resistance of the blood-vessel is insufficient and it becomes distended. This distension does not arrest the evolution of the morbid tissue, neither is the thickness of the wall of the sac in inverse ratio to its extent. Sometimes, indeed, the wall of the sac is, partially at least, much thicker than all the coats of the original vessel united. The wall of the aneurismal sac may, however, become thin at certain points and rupture, which accident is followed by an effusion of blood into the neighbouring tissues, to which the name of *false consecutive aneurism* has been given.

The sequelæ of aneurisms.—One of the most interesting points in the anatomical history of aneurisms consists in the changes they produce in the neighbouring parts by extension of their sac. In aneurisms of the arch of the aorta particularly, the bones, which cannot be pushed aside, undergo a very singular loss of substance, which the old pathologists explained by mechanical erosion. When the aneurismal sac extends to and comes in contact with the sternum, ribs, clavicle, or bodies of the vertebræ, they show excavations or loss of substance, limited by a red vascular surface. On dividing these bones, the characteristic lesions of ostitis may be distinguished with the naked eye—enlargement of the vascular or medullary spaces which are filled with fœtal medulla. This superficial observation is confirmed by microscopical examination; the osseous lamellæ are notched in an irregular manner, and the medulla, formed of young cells, no longer contains fat cells. Hence it is seen that it is not by mechanical erosion, but by a vital process, that the bone disappears; the mechanical action only determines inflammation, in consequence of which the bone is absorbed.

In consequence also of the irritation produced by pressure of the aneurismal sac, the latter may become united to neighbouring organs or canals, producing inflammatory changes in them. The inflammation of the organ at the adherent point, added to that of the wall of the aneurismal sac, softens the tissue, and perforation is produced. It is thus that aneurisms of the ascending aorta may open into the pleura, pericardium, trachea, œsophagus, superior vena cava, pulmonary artery, right auricle, or the ventricles. Adhesive inflammation of organs near to the aneurism sometimes extends to remote regions; for example, abscess of the mediastinum, or catarrhal and caseous pneumonia, may occur from aneurism of the aorta, and phlegmon of the subcutaneous connective tissue from aneurisms of the limbs.

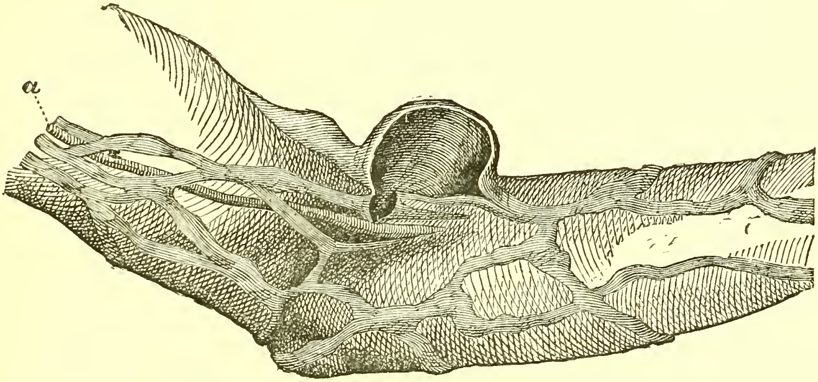


FIG. 241.—ARTERIO-VENOUS ANEURISM OF THE ARM.

Miliary aneurisms.—The different forms of aneurisms may be seen in miniature in extremely small arteries. In the small arteries at the base of the brain, and elsewhere in the same organ (Charcot and Bouchard) and in other organs, general miliary aneurisms have been described (Liouville, Meyer). Finally, dissecting microscopical aneurisms have been observed in the brain (see later, p. 623), resulting in rupture of the arterioles or capillaries, and diffusion of blood into the perivascular sheaths. These various aneurisms are generally the result either of acute or chronic endarteritis or atheroma of the arterial coats.

Arterio-venous aneurism, which consists essentially in accidental and direct communication between an artery and a vein, is particularly characterised by dilatation of the vein, and generally by the presence of an intermediate sac. The dilated vein gradually takes the appearance of an artery.

Arterial obliteration.—Obliteration of the arteries is caused by wounds which affect their coats and produce coagulation of the blood in their interior, or by ligature, torsion, pressure, or cauterisation; it may also be the result of arterial thrombosis or embolism.

Obliteration of the arteries by ligature.—Experiments on animals are necessary to observe the phenomena following ligature.

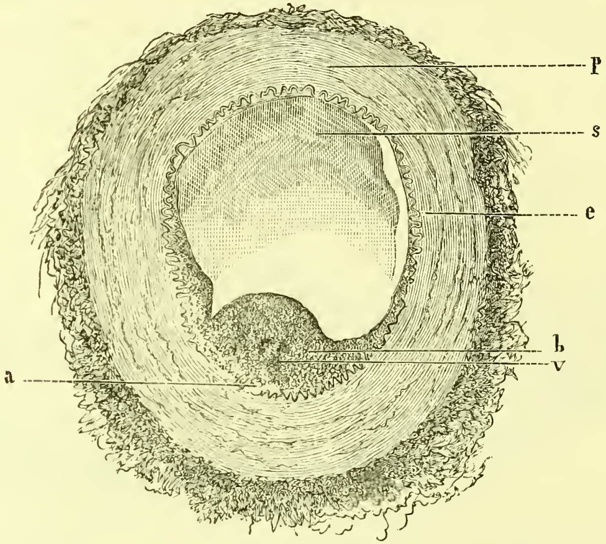


Fig. 242.—Transverse Section of the Femoral Artery of a Dog, Eight Days after Ligature.

e, Internal elastic layer limiting the middle coat; *p*, middle coat; *b*, granulation developed from the internal coat; *v*, blood-vessel of new formation supplying this granulation; at *e*, near to this bud the internal elastic layer is partly destroyed. Magnified 30 diameters.

Twenty-four hours after tying the carotid or femoral artery of a dog, a clot is formed in the proximal end of the artery and reaches as far as the first collateral branch; already the endothelium of the internal membrane shows important changes, the cells composing it are swollen and granular, and they contain one or sometimes two spherical nuclei. A few days later there is seen, particularly in the vicinity of the ligature, a thickening of the internal coat, that is, all that portion of the artery comprised between the clot and the first internal elastic lamina. In transverse sections this lamina is seen as a clear refractive and puckered band (*e*, fig. 242); it is a very important structure indicating the internal limit of the middle coat. The thickening of the internal coat is formed almost entirely of cells which appear fusiform and entangled in an irregular manner, but which are really flattened cells. These cells closely resemble endothelial cells or connective-tissue cells swollen by inflammation: they do not differ from those found in acute endarteritis. On the eighth day granulations are already found on the internal coat (*b*, fig. 242), and are very distinctly seen in transverse sections, while in longitudinal sections the internal coat seems to have gradually thickened from the upper border of the coagulum, and forms nipple-like elevations, which are particularly well seen at the level of the ligature. By the twelfth to the fifteenth day, the granulations, which originated near the ligature, are found to have continued growing on the cardiac side, and to have penetrated the blood clot, so that in transverse sections they appear like cylinders separated by blood (fig. 243). These cylinders are formed of cells separated by a

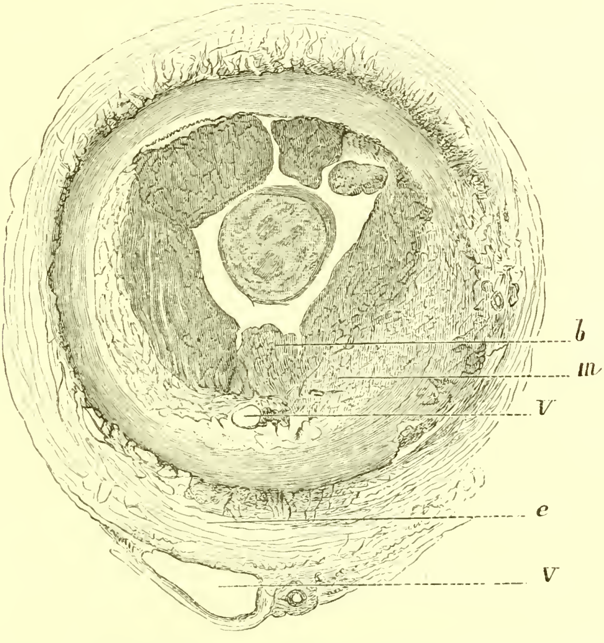


FIG. 243.—TRANSVERSE SECTION OF THE CAROTID ARTERY OF A DOG FIFTEEN DAYS AFTER LIGATURE.

b, granulations developed from the internal coat. In the centre of the figure one of these granulations is seen to be divided transversely; *m*, part of the middle layer modified by inflammation; *e*, external coat; *b*, *b*, transverse section of blood-vessels, one of which is present in the altered internal coat, and the other in the external coat. Magnified 15 diameters.

uniting substance, and contain distinct capillary vessels, filled with blood, and which are parallel to the axis of the granulation and divided with them in transverse sections. In longitudinal sections it is seen that at the point of origin of these granulations the middle coat of the artery has disappeared, so that they seem to spring from the internal coat, their blood-vessels being an extension of the vasa vasorum. Finally, these different granulations unite together, and no trace of the blood clot is left, excepting sometimes spaces filled with decolorised and granular red blood corpuscles and a few white corpuscles.

Similar preparations very probably suggested to O. Weber the idea of **organisation of the blood clot** after arterial obliteration.

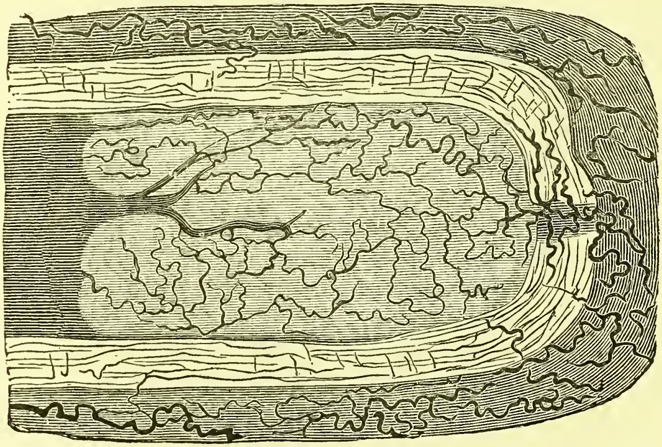


Fig. 244.—Longitudinal Section of the Ligatured End of an Artery of a Dog Fifty Days after Ligature.

The clot is injected. Magnified 40 diameters, after O. Weber.

This hypothesis, of which we long ago demonstrated the fallacy, cannot be maintained after the simple experimental analysis described above. Moreover, on examining the figures drawn by O. Weber and by those who have adopted his views, it may be seen that the pretended organised blood clot is continuous as far as the internal elastic layer, so that the internal coat with its epithelium must have entirely disappeared, or have become blended with the clot. But it has been seen that, at no period of arterial obliteration by a blood clot, is there any fusion between the granulating internal coat and the coagulated blood. Neither can we admit the explanation of Bubnoff, who, in a research prosecuted in the pathological laboratory at Würtzburg, sought to demonstrate that blood clots are actually organised, but by a process different to that imagined by O. Weber. He thought that the white corpuscles, which appear in such large numbers in the external coat in consequence of ligature, traverse the middle and internal coats to penetrate the blood clot and assist in its organisation. The experiments of Bubnoff were made on veins with a double ligature. Vermilion was sprinkled on the wound; at the end of a few days the white corpuscles, impregnated with vermilion, had penetrated through the walls of the vessel and into the substance of the clot. This fact is indisputable in *double* ligature of the veins; we have repeated this experiment with success, but in *simple* ligature of arteries and veins, though the floor of the wound was sprinkled with vermilion, we have always failed to see it pass through the walls of the vessel. Durante, who repeated these experiments with the greatest care, arrived at the same results; he admits that, in double ligature of the veins, necrosis of the coats of the vessel is produced, and that the white corpuscles then pass through them as they would traverse an inert membrane, the elements of which were dissociated by mortification.

To recapitulate, the final obliteration of arteries in consequence of ligature is produced by a new formation, the origin of which is an arteritis consequent on a traumatic lesion. As to the clot, it disappears after undergoing a series of retrogressive changes, similar to those which blood passes through when extravated into the tissues.

Obliteration of arteries in consequence of wounds.—When a small artery has been divided by a cutting instrument it gives issue to a jet of blood; if the bleeding stops spontaneously, a clot is formed in the artery as far as the first collateral vessel, and the artery is occluded. The clot commences to form at the spot where the connective tissue of the adventitious coat is divided, when the artery retracts within its sheath by reason of its elasticity. Zahn and Pitres have recently drawn attention to the peculiar mechanism of hæmostasis. Having found a very large number of white corpuscles in clots plugging arteries which were divided experimentally, they concluded that the corpuscles play an important part in the formation of blood-clots, and consequently in the vascular obliteration, that, in fact, in virtue of their adhesive properties they become blended into a solid mass, and constitute the primary hæmostatic clot. It is incontestable that blood clots formed slowly, whatever may be the cause of their formation, always contain a large number of white corpuscles, for they have been preceded by blood stasis, and this stasis is, at the same time, a cause of coagulation, and of the accumulation of white corpuscles. But it is difficult to understand how these corpuscles alone, without fibrin interposed, can form a solid mass. Whatever may be the process by which the coagulum is formed, once that it entirely fills the lumen of the vessel, it acts as a foreign body, and determines endarteritis around itself, and thus a solid cicatrix is produced by the same process as described above.

Obliteration of arteries by endarteritis and thrombosis.—Endarteritis following arterial obstruction by a blood clot has been described, but acute or chronic endarteritis may be the cause of coagulation of the blood. When at any point of an artery of middle or small calibre, such as the arteries at the base of the brain or those of the limbs, etc., the internal coat is the seat of inflammatory granulations, the vessel being almost entirely occluded by such granulations, the blood coagulates on the cardiac side as far as the first collateral branch. In chronic endarteritis, with atheromatous and calcareous degeneration, the cartilaginiform or ossiform plates are sometimes so thick, particularly in the basilar or coronary arteries, as to almost completely arrest the circulation in the vessel, and cause the formation of a clot. It cannot be doubted that in such cases coagulation of the blood is consecutive to obstruction of the artery. In delicate microscopical sections of wounds, ulcers, and chronic phlegmon, it is not rare to find arteries in which the internal coat has proliferated so as to completely obliterate the lumen of the vessel; in these granulations vascular twigs may be found, in which case the appearances are similar to those described above in ligature of arteries.

Another important cause of coagulation of blood in the small arteries is the arrest of the circulation in the capillary vessels. If, in consequence of suppuration or interstitial hæmorrhage, the blood is arrested in the capillaries by the pressure of the effusion around them, it undergoes coagulation, and the clot extends backwards into the corresponding arteriole, as far as the point where the circulation is carried on by a collateral vessel. At the point of coagulation arteritis is produced, and may become the cause of complete obstruction, or of rupture of the vessel and hæmorrhage.

Obstruction of arteries by embolism.—In the arterial obliterations hitherto studied, coagulation of the blood occurs at the point of obstruction—this phenomenon is called **thrombosis**; but when a clot formed at any point of the circulatory system, particularly in the veins, is detached by the blood current, carried into the arterial system, and arrested in an artery which it plugs, it produces what is called an **embolism**, and the migratory clot is called an **embolus.** For example, after coagulation of blood in the femoral vein, it may happen that the venous clot formed *in situ* (thrombus) may be detached, and carried by the blood current into the iliac vein, the inferior vena cava, right auricle, and ventricle, and from there into the pulmonary artery, until it reaches a ramification which it is not able to pass; it is here arrested and causes arterial obstruction by embolism. The most important phases of embolism would be easily followed in such a case, for, it being known that the patient had an obstruction of the femoral vein, the serious troubles of the pulmonary circulation rapidly ending in death would establish the diagnosis. At the autopsy, a clot would be found in a branch of the pulmonary artery, which was certainly not formed *in situ*, for it is found to correspond to a mould differing entirely in form and diameter from that of the obstructed artery. The clot itself is of a whitish or ochrous colour; sometimes it is folded on itself, and shows branches which do not at all correspond to the ramifications of the pulmonary artery. It is most frequently surrounded by a semi-coagulated mass recently formed, and in which it is imbedded; but as the embolus is firmer and older than the surrounding semi-coagulated clot, it is easily separated, when the form and calibre of the vein in which it was originally contained can be ascertained. Such is the simplest and most easily recognised case; but when the migratory clot is very small, or broken up into fragments, it is often impossible to find the embolus, which is suspected simply on account of the lesion present.

The theory of embolism has been invoked, without sufficient proof, to explain a series of anatomical changes, such as the abscesses of purulent infection and puerperal fever, though the existence of migratory clots has never been demonstrated. It is, in fact, not sufficient that the blood should coagulate and the circulation be arrested in the arteries of hæmorrhagic or purulent foci, or in infarcts, for it to be affirmed that embolism is the cause; for, as we have already seen, every interstitial hæmorrhage, and certain inflammatory conditions lead to arrest of the capillary circulation, and consequently to arterial thrombosis.

The sequelæ of arterial obstruction. Infarctus.—By using the word infarctus to signify certain lesions following embolism, Virchow has greatly obscured the subject. Before Virchow, the name was applied to a series of ill-defined changes, particularly to hæmorrhages into parenchymatous tissues, called by Lænnec foci of pulmonary apoplexy, hæmoptoic infarcts. Since then the doctrine of embolism has become generalised, and there has been a certain tendency in science to refer to embolism all what the older authors called infarctus. It is incontestible that a certain number of infarcts originate in embolism. Thus in the kidneys, spleen, liver, etc., whitish anæmic foci may be observed in the form of a cone with the base turned towards the surface of the organ, and corresponding to the distribution of an arteriole. It might be thought at first sight that the tissues contained in these foci differ profoundly from those of the affected organ; but this is not the case, for in sections made after hardening in alcohol or chromic acid, all the constituent parts of the organ are found, the elements of which have undergone fatty degeneration, and the vessels are filled with a granular mass derived from the coagulated blood. Inflammatory lesions, however, are observed around the altered parts. These infarcts are coincident with vegetative and ulcerative valvular endocarditis, with valvular aneurisms, or with chronic endarteritis. Fragments of the inflamed vascular wall or fibrinous clots have been torn off and carried into the arteries. In a few cases corresponding loss of substance may be found on the valves, but it is rarely possible to discover any migratory debris in infarctus.

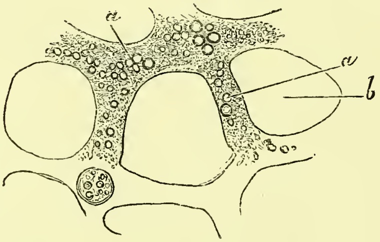


Fig. 245.

a, intertubular capillaries of the kidney filled with granular fibrin, from a case of infarctus of the kidney; *b*, section of the uriniferous tubuli.

Obstruction of an artery by embolism is followed by various lesions, as may be proved by experiment. When a single artery of small calibre is obstructed by an embolus, no lesion may be visible to the naked eye in the vascular territory of this artery; the circulation is re-established by anastomosis, the embolus acting much in the same way as a simple ligature. Thus, if a single embolic fragment (seeds of various size, drops of sealing-wax, etc.) be introduced into the lungs of a dog or rabbit, by injecting it first into the jugular vein, no pulmonary lesion appreciable to the naked eye is observed for several days following the experiment; but if a fine powder (starch or lycopodium) be injected, pulmonary congestion, hæmorrhage, and inflammation are produced in a few days.

The consequences of embolism, in arteries of the limbs and all the other organs, vary according to the size, number, and nature of the embolic fragments. Necrosis or mortification generally occurs when many embolic fragments are distributed in the arterial system of the limb, in such a manner that collateral circulation is impossible. In organs in which the vascular supply is limited, a single embolic fragment may produce the same results, as may be observed in the kidney, spleen, liver, and brain; but in the limbs a single embolus cannot produce gangrene any more than ligature of an artery. If the embolus has irritating properties, which almost all solid foreign bodies possess, suppurative inflammation is produced *in situ*, which does not differ from that caused by the same foreign body if introduced into the cellular tissue; phlegmon hence results. The walls of the artery at the level of the embolus are compressed, and undergo necrosis and purulent infiltration, followed by inflammation of the neighbouring connective tissue. When, on the contrary, the embolus is derived from the organism, as, for example, a simple fibrinous clot from the heart, it obstructs the artery and causes coagulation of blood as far as the first collateral branch. The process of organisation, which ends in the complete obliteration of the artery, does not differ from that following ligature: it is affected by endarteritis, while collateral circulation re-establishes the course of the blood.

In embolism of the arteries of the kidney, spleen, liver, and brain, the initial phenomenon is a swelling limited to the area supplied by the obstructed artery; the tumefied part is of a violet-red colour. The blood accumulated in this vascular area stagnates, and later undergoes coagulation. At this stage the lesion, which is in the form of a cone, is called **red infarctus**; it is composed of the elements of the tissue and coagulated blood, forming a mass in which life is extinct. The blood undergoes the usual metamorphoses, and the parenchymatous cellular elements undergo fatty degeneration. The infarctus then becomes yellowish-white in colour, while it still remains tolerably firm, though a little shrunken. **Yellow infarctus** forms such a distinct mass that it might be mistaken for a tumour, if it was not conical in form, with the base turned towards the periphery of the organ. On examining delicate sections under the microscope, the perfect tissue of the organs will be recognised, only the vessels are found injected with a granular mass (*vide* fig. 245) caused by transformation of the blood, and the parenchymatous cells are infiltrated with fat granules. On the borders of **white infarctus** the blood-vessels of the living parts are dilated and filled with blood; the connective tissue is infiltrated with white blood corpuscles, and more or less extensive areas of interstitial hæmorrhage are frequently found. The parenchymatous elements, the epithelial cells of uriniferous tubuli, or the hepatic cells, for example, show multiple nuclei and often fatty infiltration, and in the kidney the tubuli contain casts of fibrin, blood, and white corpuscles.

In the third stage, white infarctus softens. This softening, which commences at the centre, causes the molecular destruction of all the necrosed parts; they are then taken up by the lymph vessels of the connective tissue, which is developed as a kind of cyst round the mortified part. This phenomenon is very similar to that already described as occurring in caseous gummata (*vide* p. 197 and fig. 107). A softened infarctus often becomes infiltrated with calcareous granules, dries up, and is transformed either into a dry atheromatous mass, or becomes actually petrified. Finally, all the necrosed part may be absorbed, a stellate cicatrix being left in its place. The death of a more or less extensive part of an organ, without the production of true gangrene, has been called *necrobiosis* by Virchow.

The miliary or larger abscesses, observed in infectious diseases, particularly in purulent infection, and which were for a long time referred to capillary embolism, are due to the fact that the blood contains infectious microbia.

Fatty emboli.—Fatty emboli of the blood-vessels of the lung, discovered by Zenker in 1862, have been the subject of a series of researches by Lücke, Recklinghausen, Flournoy, Cohnheim, and

Egli-Sinclair, and of papers read at the Société Anatomique, particularly by Déjerine. In surgical diseases of the bone, particularly those resulting from comminuted fractures, inflammation of the osseous medulla, and inflammation and wounds of parts rich in fat, fatty emboli of the pulmonary blood-vessels are frequently observed. These vessels are then found to contain a considerable quantity of fat, which does not however produce infarcts or pneumonia, but simply pulmonary congestion and œdema. The respiratory troubles and asphyxia which result are frequently the cause of sudden death, particularly when the capillary vessels of the lung are affected for a great extent. If recovery takes place, which may be observed if the pulmonary vessels are not loaded with fat, the latter is gradually eliminated, particularly by the kidneys. The recognition of fatty embolism is easy either in sections of the lung cut in the fresh state and stained with osmic acid, or in preparations made after hardening fragments of the lung in osmic acid.

Amyloid degeneration of the small arteries.—We have already described on page 69 the general appearance of amyloid degeneration of the arterioles, and have insisted on the fact that the middle coat of the small arteries is particularly liable to this form of degeneration. The muscular elements of this coat first become infiltrated with amyloid matter, but they preserve their form and relations, so that the change is not recognised, excepting by employing the reagents iodine or the violet of methylanilin. In some cases an organ treated by iodine shows an arterial network so perfectly coloured that it seems to have been injected. When the change is very advanced, the muscle cells, hitherto distinct, become fused into a single mass, the wall of the arteries appearing to be formed of a homogeneous and thick membrane. The calibre of the blood-vessel is narrowed, so that the circulation of the blood may be arrested.

The organs most frequently affected with amyloid degeneration of the arteries are the spleen, liver, kidneys, intestinal mucous membrane, and the lymphatic glands. It is observed in consequence of prolonged suppuration in phthisis, syphilis, etc.

Tumours of the arteries.—Primary tumours of the arterial system are limited to the new formation of arterial tissue in the dilatations and elongations of arteries of simple angiomata, and to a peculiar form of angioma, namely *arterial varix*, or *cirsoid* *aneurism.* In these tumours the arteries are dilated, elongated, serpentine, and thickened; they present numerous anastomoses and partial dilatations; they are usually located in the temporal and occipital arteries.

The arteries which supply a certain number of tumours, for example those of the mamma, thyroid body, etc., are extremely hypertrophied, and there is an actual new formation of arteries taking place simultaneously with the growth of the tumour. This new formation seems to be produced by a transformation of the capillaries into arterioles and larger arteries by the formation of smooth muscular elements developed from the embryonic cells surrounding the vessel. This evolution is, however, extremely difficult to follow, and there is still much uncertainty regarding the subject.

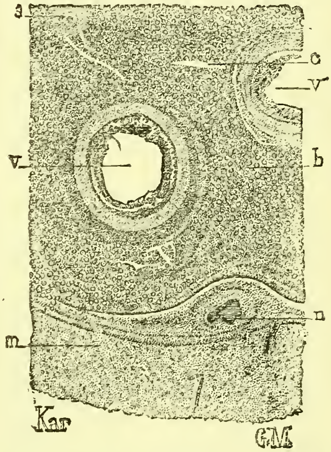


FIG. 246.—SECTION OF TUBERCULAR MENINGES.

a, small obliterated vessel; v, v, much larger vessels. The internal coat of these veseels is greatly thickened, and in the internal layer of the vessel which is in the centre of the figure are seen two giant cells; *n*, vessel obliterated near the cerebral substance *m*. Magnified 40 diameters.

Tumours, which develop rapidly round an artery of a certain calibre, determine phenomena in every way resembling those of arteritis, that is to say, the vegetations of endarteritis, disappearance of the middle coat, and an embryonic condition of the external coat. In arteries thus degenerated blood clots are frequently formed, or hæmorrhage occurs due to rupture of the friable arterial coats. These lesions are particularly observed in rapidly growing sarcoma or carcinoma: the tissue of the tumour may often be seen to grow into the blood-vessel after the middle coat has disappeared. When the circulation is impeded or arrested by these lesions of the arteries, the part supplied by them becomes mortified. If the mortified part is superficial, as occurs in tumours of the cervix uteri, it softens and ulcerates, and if the necrosed mass is located in the substance of an organ it produces a caseous focus.

It is not rare to see tubercular granulations develop in the tunica adventitia of arterioles. Mugge has also described tubercular granulations in the internal coat of the pulmonary artery, as well as in the pulmonary veins of tubercular lungs. One of us has observed, in a case of tuberculosis of the cerebral meninges, a lesion of the arterioles consisting in a peculiar form of endarteritis, characterised by the thickening of endarteritis, and by the new formation of a large quantity of cells of various forms in the thickened artery. In the midst of these cells there were a number of very large giant cells (*b b*, fig. 247); the endothelium was perfectly preserved on the surface of the new formation developed in the internal membrane. The final lesion of such a process is the obstruction of the small artery, coagulation of the blood, and subsequently complete obliteration.

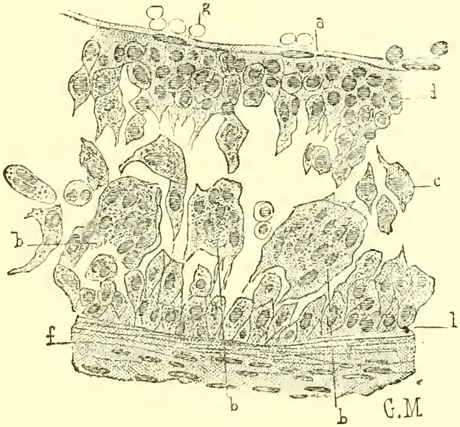


Fig. 247.—Section of Inflamed and Tubercular Internal Coat.

a, layer of flat endothelial cells indicating the internal border of the inflamed inner coat; *g*, red blood corpuscles circulating in the lumen of the vessel; *d*, layer of round or polygonal cells; *b*, *b*, *b*, giant cells; *l*, layer of cylindrical and round cells at the base of the inflamed inner coat; *f*, middle coat. Magnified 200 diameters.

CHAPTER X.

LESIONS OF THE CAPILLARY VESSELS.

I. Normal Histology of the Capillaries.

THE capillary vessels are essentially formed of endothelial cells united at their edges, and arranged in such a way as to form a network of anastomosing capillaries (*vide* p. 38). The capillaries have everywhere the same structure, but their size and the arrangement of their networks vary in each organ and in each tissue. The vessels are surrounded with fasciculated or reticulated connective tissue, or they are contained in lymph spaces. In fasciculated connective tissue the capillaries, lined with flat cells, are found in the spaces of this tissue, alongside the fasciculi without adhering to them, the lymph being in direct relation with the vascular wall; so that in reality a capillary of the connective tissue is situated in a lymph space. This arrangement does not only exist in the subcutaneous cellular tissue, but in the skin, muscles, nerves, and cellular tissue of the organs. In the lymphoid organs—lymphatic gland, follicles of the intestines, tonsils, glomeruli of the spleen, thymus, etc.—the capillaries are covered with a dense fibrillated layer from which the fibrils of the stroma spring. The lymph bathing this stroma is thus separated from the blood current by two layers, the cellular membrane of the capillary, and its reticulated investment. The capillaries of the glands are placed in the lymph spaces which surround the acini, and separate them from neighbouring acini; those of the nervous centres are contained in perivascular sheaths.

When a capillary occupies a lymph space, it is generally covered with a layer of endothelium, and is connected to the wall of this lymph space by bands of connective tissue, varying in thickness. From the constant existence of lymph spaces between capillaries and the constituent elements of the tissues and organs, it results that these elements are not in direct relation with the plasma of the blood, but that this plasma is first effused into the lymph spaces and absorbed by the elements found in these spaces, according to their physiological or pathological needs. It must not nevertheless be concluded that the exuded fluids have no influence on the functions of these elements: we have, in fact, shown, when considering œdema, the modifications of flat connective-tissue cells, under the influence of a morbid serous exudation into the connective-tissue spaces. To recapitulate, it is not the blood which is the vehicle of nourishment to the elements, but the lymph derived from the blood.

II. Pathological Histology of the Capillaries. Inflammation of the Capillaries.

We will not here reconsider in detail the changes observed in inflamed vessels, and which have been already described (*vide* p. 109), but we propose to point out the peculiar alterations of capillaries in inflammation. The capillaries of inflamed vascular tissues present two orders of phenomena; some consist in the modification of their wall, others in the extension of the old vessels and a new vascular formation. At the commencement of inflammation swelling of the endothelial cells of the capillaries is observed; the cells which were flat, homogeneous, and could not be distinguished, then appear granular, and seen sideways they seem fusiform and distinct from one another. This arrangement is particularly well seen in transverse sections of inflamed vessels (*vide* fig. 249). In the mesentery of a frog which has been exposed to the air it is much more difficult to see the swelling of the cells, which may be, however, recognised with attention. Separation of the cellular elements results in dilatation of the capillary vessels, and also facilitates the escape of the white and red corpuscles and of the fibrinogenic plasma.

In chronic inflammation of the mucous membranes, notably in catarrh, dilatation of the capillary vessels is considerable. In such cases the dilated capillaries remain full of blood after death, and are seen as spots or red markings, while normal capillaries are generally emptied in consequence of the contraction they undergo after death. This fact alone shows that blood-vessels, modified by inflammation, have lost one of their most important properties, that of elasticity.

Modifications of the vascular walls, joined to increase of the blood pressure, cause various accidents, observed particularly in the brain. In the foci of softening and hæmorrhage of this organ, or more particularly round these foci, small red spots or nodules are often seen, and which are due to dilated capillaries or to effusion of blood into their perivascular sheaths. The latter lesion is very frequent, and has been called by Kölliker and Pestalozzi by the name of *dissecting aneurism of the capillaries.*

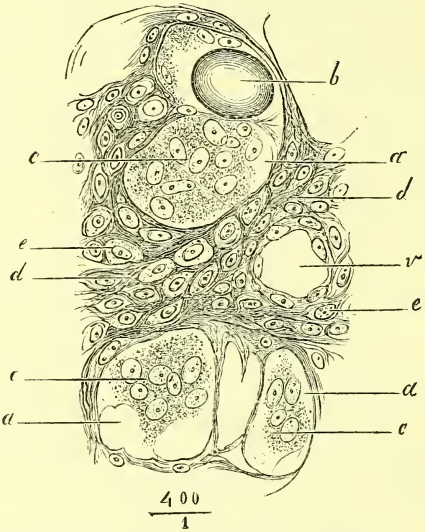


FIG. 248.—INFLAMED CONNECTIVE TISSUE.

a, space occupying the place of adipose cells the fat of which has been absorbed, and now filled with young nuclei, *c*, surrounded with granular protoplasm ; *e*, embryonic cells ; *v*, vessel, the wall of which is formed of tumefied endothelial cells.

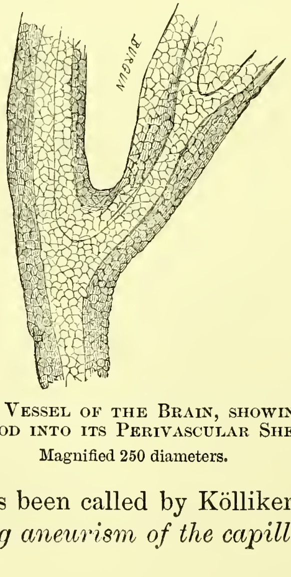


FIG. 249.—CAPILLARY VESSEL OF THE BRAIN, SHOWING EXTRAVASATION OF BLOOD INTO ITS PERIVASCULAR SHEATH.

Magnified 250 diameters.

As to the **miliary aneurisms of the brain**, described by Charcot and Bouchard, they are more frequently produced by dilatation of the arterioles than of the capillaries. They seem to be the result of inflammation located in the wall of the vessel itself, and from this point of view their pathogenesis does not differ from that of aneurisms of medium calibre. They are fusiform or sacculated, and are almost always accompanied with hæmorrhage into the perivascular sheath, being, therefore, at the same time simple and dissecting (*vide* fig. 250).

Regarding the new formation of vessels in inflamed tissues we have nothing to add to what has already been said in the chapter on inflammation, page 109.

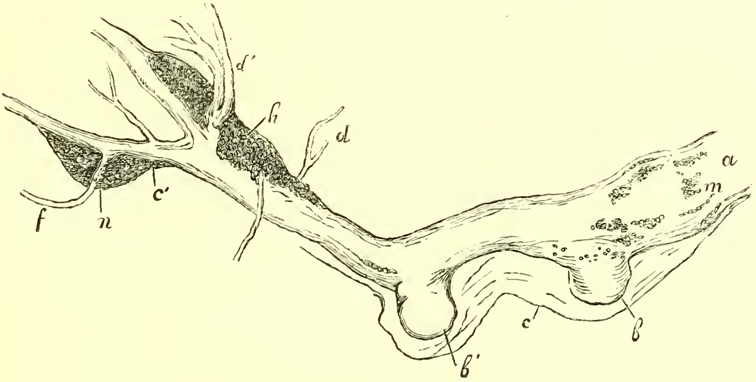


Fig. 250.—Miliary Aneurism of an Arteriole of the Brain.

a, trunk of the arteriole showing the granules *m*; *c*, perivascular sheath; *b*, *b′*, aneurisms formed by a uniform dilatation of the arterial coats; *n*, *h*, effusion of blood into the perivascular sheath *c′*; *d*, *d*, *f*, capillary branches springing from the arteriole. Magnified 30 diameters.

Nutritive lesions of the capillaries.—The most frequent lesion of the capillaries consists in fatty degeneration of their walls. It is met with in all vascular organs, but it is particularly frequent in the kidney and the nerve centres; it may be observed whenever nutrition is lessened or arrested, and it then accompanies fatty degeneration of the elements composing the organs. In the brain and spinal cord, however, of new-born infants, and during the first month of life, a great number of granular bodies are found in the capillaries. In cerebral softening, the capillaries of the brain, which normally often contain in the adult a few disseminated refractile granules, are loaded with fat granules, which at certain points give the capillary the form of a dark granular cylinder. The perivascular sheath contains blood and granules of hæmatoidin (*vide* fig. 251), which indicates that there has been diapedesis, or rupture of the morbid capillary vessel. At other times, the perivascular sheaths are dilated and contain granular bodies (*vide* fig. 252), in which a nucleus may almost always be discovered, on staining the preparation with picrocarminate of ammonia. These granular bodies are either lymph cells loaded with fat granules, or endothelial cells of the perivascular sheath which have undergone the same alteration. After section of nerves, the capillaries of the peripheral segment also undergo fatty degeneration: the same change is observed in the neighbouring connective-tissue cells and migratory cells. In infarcts following obliteration of arteries, in chronic inflammation with consecutive fatty degeneration, in Bright's disease particularly (*vide* fig. 253), and in tumours which have undergone the same change, fatty degeneration invades the walls of the capillaries.

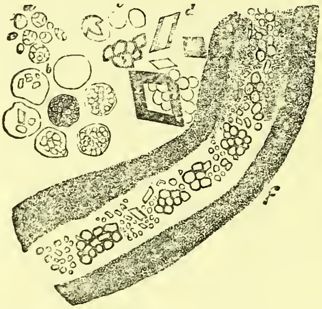


Fig. 251.—Crystals of Hæmatoidin.

a, free crystals; *b*, crystals contained in cells; *f*, capillary vessel containing granules of hæmatoidin.

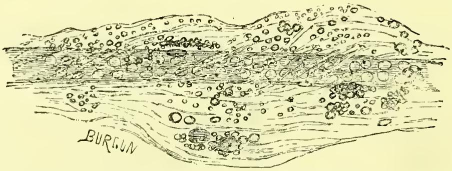
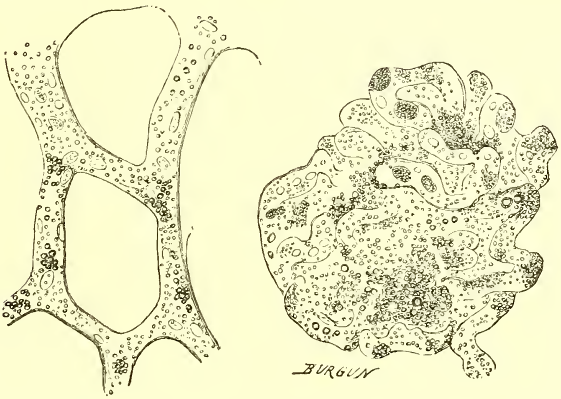


Fig. 252.—Capillary Vessel of the Brain, in the Distended Sheath of which are seen Free Fat Granules and Lymph Cells surrounded with Fat Granules.

Magnified 250 diameters.

Calcareous degeneration is rarely seen in capillaries. Calcareous salts are, however, met with, either in the form of granules or plates, particularly in angiolithic sarcoma of the dura mater. Also, sometimes, in angiolithic sarcoma, or in chronic encephalitis, in general paralysis, for example, segments of capillaries are found infiltrated with calcareous salts. They appear vitreous and brittle, and are often broken up.

Amyloid degeneration transforming the capillaries into vitreous tubes is frequent. The hypertrophy of the amyloid wall is sometimes so great as to transform the vessels into solid homogeneous, vitreous cylinders, much larger in diameter than normal capillaries. In this change the endothelial cells of the capillaries are preserved for a long time. This form of degeneration is particularly well marked in the liver and kidney, and principally in the vessels forming the Malpighian tufts: sometimes the change is only found in the glomeruli, while in other organs amyloid change more frequently commences in the arteries.



FIGS. 253 AND 254.—FATTY DEGENERATION OF RENAL VESSELS IN A CASE OF BRIGHT'S DISEASE.

On the left is part of the capillary network in a state of fatty degeneration, and on the right a glomerulus of Malphigi, showing similar lesions. Magnified 250 diameters.

We will not reconsider the changes of the capillaries in the different kinds of tumours, simply recalling that in sarcoma, as in all inflamed tissues, the capillary wall returns to the embryonic condition.

CHAPTER XI.

LESIONS OF THE VEINS.

I. Normal Histology of the Veins.

The three coats, generally admitted in the veins, are much less defined than those of the arteries; moreover, veins of the same calibre have not, in different regions of the body, always the same structure, inasmuch as the muscular and elastic elements have neither the same arrangement nor the same thickness. The internal coat of veins is composed of flat cells separated by a fibrillated substance, and is lined with flat polygonal endothelial cells, shorter than those of the arteries. The middle coat commences by circular elastic fibres or laminæ, and from this first elastic layer spring elastic fibres, which form a network, in which are arranged the smooth muscle cells and connective-tissue fasciculi. The line of demarcation between the middle and external coat is not clearly marked, but all that part of the vein which contains muscular fibres may be looked upon as the middle coat. We should add that veins which have no elastic fibres—the sinuses of the dura mater, subclavian veins, and veins of the retina—have no middle coat.

As there are no elastic laminæ in the middle coat of veins, it is easily understood how that their walls allow of the passage from without inwards of fluids, or from within outwards of plasma and blood corpuscles. If absorption is much more easily accomplished by the veins than by the arteries, as Magendie showed, this is not only due to the fact that the blood current is slower, but also that the venous walls are much more easily traversed. Diapedesis, which is very frequent in the walls of the veins, is exceptional in the arterial coats.

The elastic framework of the middle coat of veins of large and medium calibre forms a close network near the internal coat, and becomes more and more open as the external coat is approached. The muscular fibres have in the middle coat a longitudinal or transverse direction, according to the vessels under consideration; thus, in the inferior vena cava, portal and renal veins, the internal fibres are circular, and the external longitudinal; the femoral and popliteal veins have an internal longitudinal layer; the arrangement of the muscular fibres is still more complicated in the saphena veins, in which may be remarked an internal longitudinal layer, then a series of transverse and longitudinal layers superimposed. The veins of the neck have only a few scattered muscular fibres situated in the first elastic meshes external to the intima.

The valves of the veins are extremely thin, though they are formed of many distinct layers. Besides the endothelial lining which covers the two surfaces of the valve, three layers may be distinguished, two superficial and one intermediate. The internal, the valve being raised, is of the same structure and thickness as the internal coat of the vein; it is continuous at the free border of the valve with the external, which is, however, much thinner. This arrangement is similar to that of the sigmoid and auriculo-ventricular valves, in which the endocardiac layer, which receives the friction of the blood at the level of the endocardiac orifices, is much thicker than the other. The intermediate layer is an expansion of the middle coat, and like this contains a few muscle cells, but only at its base.

The **vasa vasorum** are found in the veins wherever fasciculated connective tissue is present, and they penetrate into the substance of the middle coat.

II. Pathological Histology of the Veins.

Inflammation of the veins. Phlebitis.—Spontaneous phlebitis is hardly ever met with except in the veins of the uterus in consequence of pregnancy. Phlebitis is generally complicated with inflammation of the surrounding connective tissue, or it occurs in consequence of wounds, ligature of veins, and primary coagulation of blood in their interior, or thrombosis. In wounds of the veins, coagulation of blood and phlebitis occur together, so that the phlebitis is dependent, at least partly, on the thrombosis.

In **ligature of a vein**, an almost obsolete operation in surgery, but which may be performed experimentally on animals, the blood coagulates in its peripheral end, as far as the first collateral branch, a clot being also formed in its proximal end. During the first few days nothing is seen but swelling and multiplication of the endothelial cells. Soon, however, the entire internal coat swells, in consequence of the production of new cells which form granulations, particularly well marked at the level of the ligature. Later, these granulations become vascular, unite together, and complete obliteration of the vein takes place, exactly as in the arteries. If, as Bubnoff showed, a segment of the jugular vein of the rabbit be included between two ligatures, and vermilion be sprinkled on the wound, the pus cells found in the external coat and neighbouring connective tissue are full of granules of vermilion; the corpuscles carrying the vermilion are then found throughout the thickness of the vein, on its internal surface as well as in the interior of the clot; but if, instead of a double ligature, a simple ligature only is practised, and vermilion sprinkled on the wound, it does not penetrate to the interior of the vein, nor reach the clot. We have already spoken of these experiments when treating of arteries (*vide* p. 511). Blood clots in veins do not undergo organisation any more than in arteries: they break down into a granular detritus and disappear gradually.

Wounds of veins.—The simplest wound of a vein is that made in the operation of bleeding from the arm; the wound made, implicating both the vein and the skin, unites by first intention, though, as has been already explained, such union is not effected without inflammation playing an important part. A thin blood clot is left between the two lips of the wound; the following day redness and a slight œdematous tumefaction are observed; towards the fourth day the scab formed over the incision falls, and cicatrisation is complete. These simple phenomena have, however, not yet been studied histologically, but it is probable that union of the vein occurs, as in connective tissue of the skin (*vide* p. 413), by the interposition between the lips of the wound of embryonic connective tissue, and by its organisation into ordinary connective tissue.

In a wound, if the connective tissue of the external coat of a vein participates in the inflammation, it becomes infiltrated, for a variable extent, with embryonic and pus cells. In inflammation, ending in the formation of abscess, the external middle and internal coats of the vein may all become ulcerated and destroyed. This ulceration, which is particularly observed in abscesses of the axilla, groin, and posterior mediastinum, is accompanied with coagulation in the interior of the vessel, the danger of direct introduction of pus into the circulatory system being thus avoided. Sometimes, however, the clot is insufficient, and the accidents of septicæmia and pyæmia take place; at other times, the clot undergoes changes, it softens at the centre, and at its cardiac end an irregular canal is formed which brings the focus of suppurative inflammation into communication with the vascular system. The losses of substance observed in such cases, in the walls of the veins, are more or less extensive; the vein is blended by its external coat with the phlegmonous tissue surrounding it, it cannot therefore contract on being cut, but remains gaping like the hepatic veins. The external border of the loss of substance is thus confounded with the indurated or fungoid layer limiting the purulent focus. On the side of the cavity of the veins the loss of substance is more defined, although at this point the various coats are infiltrated with pus, and consequently thickened or partially necrosed. This infiltration of the venous wall is easily recognised under the microscope by the presence of pus cells, but, as the inflammatory process has been rapid, organised vegetations are not produced in the internal coat of the vessel.

In positive wounds of vessels, as those made in surgical operations, particularly in amputations, all the blood contained between the point of division and the nearest valves flows out, and this segment of the vein remains empty. A clot is formed above the valves as far as the first collateral branch. The empty extremity of the vein participates in the inflammation of the wound, and adhesive periphlebitis and endophlebitis take place as after ligature, obliteration of the vessel being the consequence.

Hitherto we have seen coagulation of the blood accompanying phlebitis; till recently it was thought that coagulation of the blood in the veins was always caused by phlebitis. Virchow has attempted to prove that primary phlebitis is extremely rare, and that, when a clot and phlebitis are both produced in a vein, coagulation has most frequently preceded the inflammation. This theory, which seems to us to be too absolute, has been accepted by all German pathologists; it has, however, the merit of inducing careful study of the condition of the formation of blood clots in the veins.

Venous thrombosis.—The causes of venous thrombosis are of two kinds: slowing and arrest of the circulation, or changes in the internal coat of the veins. On arrest of the circulation after death, the blood which is accumulated in the venous system undergoes coagulation. Pathologists should be well acquainted with these post-mortem clots, so as not to mistake them for those

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of thrombosis. They are chiefly found in the large veins, the vena cava, iliac veins, etc. These post-mortem clots only occupy a small part of the lumen of the vessel; they never fill it, are not adherent to the wall, and they send long prolongations into the collateral branches. They are of a reddish-brown colour, veined with white, and are partly fibrinous, partly cruoric, the upper layer is generally white or pink, the lower layers red, owing to the dorsal position of the cadaver. These clots vary greatly in thickness in the same vein, when recently coagulated they have the consistence of fibrin.

Thromboses occurring during life are due to arrest, or impediment of the local or general circulation. Thus asystole causes the formation of clots in the right heart and large veins. It is thus also that tumours and abscesses are often the cause of coagulation of the blood in the veins with which they are connected. Pressure of the gravid uterus acts in the same way on the hypogastric and iliac veins, etc. Slowing of the blood in varicose dilatation may also be the cause of thrombosis. When the circulation of the blood is impeded or arrested in the capillaries of a region, the vein carrying away the blood may also be the seat of thrombosis; thus in pneumonia clots may be formed in the pulmonary veins, by the pressure exerted on the capillaries by the exudation distending the alveoli. Thromboses of the veins of the kidney and spleen, in caseous infarctus, etc., are also produced by stasis of the capillary circulation. It is the same in leukæmia; the capillary circulation being impeded by the large number of white corpuscles, blood clots are formed in the veins.

In thrombosis occurring during life, the clot completely fills the vessel, is adherent to its wall, and terminates towards the heart in a point or groove. It is formed of a series of nested layers, of which the most superficial are the most recent, and may be still cruoric, while the central and middle layers are of a grey or yellowish colour. When the clot is old, at its centre is often found an anfractuous cavity filled with a fusiform, whitish, opaque detritus. Under the microscope this detritus is seen to be composed of a number of white corpuscles in a state of caseous degeneration, they are irregular in shape, the nuclei are no longer apparent, but fat granules are seen in their interior; beside these corpuscles are found granules, which disappear when acted upon by acetic acid, and free fat granules. A section of the clot, cut after hardening in alcohol, stained with carmine and examined in acidified glycerine, shows red blood corpuscles still recognisable at the periphery of the thrombus, separated by layers of fibrin in which are seen white corpuscles stained red by the carmine. In the interior of these layers the fibrin forms still closer laminæ, between which are seen granular collections containing masses of pigment of different shapes and sizes.

In the clots of spontaneous thrombosis of veins there is always a large number of white corpuscles, a phenomenon which can be attributed neither to the new formation of these elements nor to their migration. We have already shown that whenever the blood current is slowed in a vessel, the white corpuscles accumulate*:* now, since thrombosis is preceded by slowing of the circulation, this condition favours both accumulation of leucocytes and coagulation of the blood; hence therefore it is quite natural that in blood clots formed spontaneously during life a large number of white corpuscles should be present. They become free in the centre of the clot when the fibrin breaks down.

The arrangement of the thrombus in concentric layers is due to the fact that the primitive clot, which is formed of blood coagulated in the vein, undergoes contraction throughout its whole extent, leaving, therefore, a space between itself and the wall of the vein, through which the blood passes, but with difficulty; it therefore coagulates, and coagulation is again followed by contraction, and the same phenomena are repeated till the distended vein exactly fits the clot, when circulation is arrested. Until the coagulum entirely fills the vein, it is frequently retained *in situ*, by the prolongations it has sent into the collateral veins; this explains why a thrombus is not often detached and thrown into the blood current.

Whether **phlebitis** be primary or consequent on thrombosis, it produces a series of inflammatory alterations in the diseased vein, similar to those produced in inflamed arteries (p. 491). Swelling and proliferation of the endothelial cells is first observed; the entire internal membrane soon participates in the inflammation, and it thickens either regularly or in the form of granulations. The thickening is due to the new formation of numerous cells, some round similar to lymph cells, others elongated, fusiform, or flattened. Five or six days after the commencement of this endophlebitis, capillaries of new formation are already visible in the internal membrane; they are most probably developed from the large fusiform cells just spoken of. These *vaso-formative cells* unite by means of their thread-like protoplasmic processes, and form a network, or else they are arranged one after another and form embryonic capillaries perfectly distinct and easily recognised, even when they contain no red blood corpuscles. These capillaries anastomose with the vessels of the middle coat, and circulation of the blood is thus established in the morbid internal membrane. This membrane is often continuous, without a definite line of demarcation, with the fibrinous portion of the clot; the newly formed capillaries may even penetrate into the midst of the fibrinous trabeculæ. Fine fibrils of connective tissue soon show themselves in the thickened internal membrane, and a fibro-vascular growth is produced which surrounds the fibrinous clot.

The circulation of the blood and the arrangement of the blood-vessels in the internal coat deserve a special description. At the base of the thickened internal coat, and quite close to the internal limit of the middle coat, may be observed large sinuses or lacunar spaces, which receive the blood from the capillaries of the middle coat. These sinuses are lined with an endothelium, and their walls are simply formed by the adjacent connective tissue. They give origin to a network of fine capillaries, which send ramifications throughout the internal part of the thickened internal membrane. The circulation of the blood in this new system, composed of afferent capillaries, cavernous lacunæ, and efferent capillaries, is effected easily and regularly, the proof of which is given on microscopical examination, for all the vessels are found filled with normal corpuscles.

In the external coat also new cellular elements may be seen between the fibres, and it is decidedly swollen—*periphlebitis*. The middle coat does not generally undergo change; in cases, however, in which the inflammation is very acute, the wall of the vein may be the seat of true suppuration, which may invade even the middle coat. Thrombosis may thus become the origin of a peripheral venous abscess.

Suppuration is far from being the usual termination of thrombosis; sometimes the blood clot is partly or entirely detached, and the blood current, re-established in the vein, bears along the thrombus, which finally obstructs a branch of the pulmonary artery, if it was formed in the general venous system, or an artery of the aortic system, if it originated in the pulmonary vein. Phlebitis rather frequently terminates by cavernous change of the vein. After absorption of the clot, the thickened internal membrane fills up all the original lumen of the vessel, but its blood-vessels may dilate at the same time that the septa separating them become thinner, from which it results that the connective tissue plugging the vein is traversed by lacunæ full of blood, recalling the structure of certain cavernous angiomata (Pitres). The most frequent termination of venous thrombosis is, however, the definite obliteration of the vein, which is then transformed into a fibrous cord.

Varix.—The term varix is given to a dilatation of veins accompanied with persistent modifications of their walls. The word varix is not absolutely synonymous with phlebectasis, for simple dilatation in phlebectasis may be seen, for example, around tumours, without varix being present; indeed, if the tumour be removed, the simply dilated veins return to their original condition. Varices are especially observed in the superficial veins of the lower limb. To understand the arrangement of varicose veins, they should be dissected out throughout their whole length; they are then found to be not simply dilated, but much more elongated and tortuous than examination of the living subject would have led one to suppose. The calibre of these veins is very irregular, and fusiform or ampullar dilatations are observed; their walls have not everywhere the same thickness; their valves are incompetent, and are often reduced to narrow bands flattened against the wall, or partly destroyed. At their level, considerable thickenings, in the form of nodules, are generally observed. The vein shows on its internal surface longitudinal projections and depressions. Its wall is thickened in places, so that in dividing the vein transversely it remains gaping like an artery.

Calcareous incrustations in the form of plates, nodules, or nested balls are formed in the coats of varicose veins. Small calcareous plates are not always visible in a vein in the fresh state, but after dessication the calcified parts become evident by their opacity and prominence, while the adjacent parts have contracted and become transparent. Calcareous infiltration is seen in the form of balls or **phleboliths** in the varicose diverticula; but calcareous induration of a vein may be seen for a length of several centimeters, the vein being then transformed into a solid tube with ramifications, continuous with other varicose veins.

When varices are old, and have reached a high state of development, the dilated tortuous veins form a kind of cavernous tumour with large meshes; they are folded on themselves, and mixed with a mass of connective tissue, so that it is difficult, sometimes even impossible, to isolate them ; it is equally impossible to dissect them out, and to separate the wall of each one of the veins constituting the tumour. Around all old varices the subcutaneous cellular tissue has undergone the changes of chronic inflammation ; it is infiltrated with fluid, is very vascular, and of a lardaceous consistence.

To make a histological examination of varicose veins, the process already described for arteries should be employed, that is, dessication, transverse or longitudinal section, staining with carmine, and preservation in glycerine, to which formic acid is added. The changes shown consist in hypertrophy of the middle coat, caused by multiplication of its muscular elements, and particularly by a new formation of fibrous tissue. The internal coat is not sensibly hypertrophied, vegetations are also not generally found on its internal surface, except near the insertion of the valves, and when there has been coagulation of the blood. This coat has the appearance of a band formed of two or three rows of lenticular nuclei, and it stains slightly with carmine. Beneath is an elastic network, the meshes of which are filled with large fasciculi of connective tissue, generally having a direction parallel to the axis of the vessel; it is these which produce the longitudinal prominences seen with the naked eye on the internal surface of the vein. To this internal layer of the middle coat, which is always of considerable thickness, succeed fasciculi of muscular fibres, which in longitudinal sections of the veins appear as islets formed of a series of clear circles showing centrally the section of a nucleus. In the external layer of the middle coat these fasciculi have almost all a transverse direction, and intersect the longitudinal fasciculi at right angles. They are generally separated from one another by connective tissue, so that this tissue is continuous without interruption from the internal coat to the external. Between the connective-tissue fasciculi, granules or masses of granules of blood pigment are often observed, which show that the venous wall has been infiltrated with red blood corpuscles. The middle coat, thus modified, is from two to ten times thicker than normally.

The trunk of the vein does not alone undergo dilatation, but all its branches, and even their vasa vasorum. These minute vessels then become tortuous and dilated, and their walls thickened ; when the dilatation of a vein is very marked, they may acquire a considerable diameter in the substance of the middle coat, and extend to its most internal layer; sometimes the dilated and tortuous vasa vasorum form in conjunction with the principal vein very complicated cavernous tumours.

The **calcareous plates of veins** are developed in the fibrous and internal portion of the middle coat; calcareous granules are first deposited in or between the fasciculi of connective tissue; they soon increase in size, and join together to form transparent plates, grooved with irregular, opaque, and granular striæ.

Instead of being regularly dilated, varicose veins are more frequently enlarged only at certain points of their course, and present fusiform or sacculated dilatations. At these spots their walls are much thinned, and in sections comprising their entire thickness changes similar to those of the arterial walls in an aneurismal sac are observed. The muscular coat has more or less entirely disappeared, only a few scattered fragments of it remaining, and the blended external and internal coats alone constitute the wall of the dilated vein. These varicose sacs may become so thinned as to rupture and cause hæmorrhage.

The indurated connective tissue and hypertrophied skin near varices show the histological alteration of chronic phlegmon or elephantiasis. Small purulent foci are often formed which unite and open, leaving an ulcerating wound, the base and edges of which are indurated; these ulcers then continue to enlarge and, blending with others, may attain considerable size. The inflammation often gains the surface of bones and causes osseous growths in the form of stalactites, sometimes of great extent.

Tumours of veins.—Primary tumours are not observed in veins, with the exception of angioma which is developed in their walls (p. 239). Secondary tumours of veins are, on the contrary, frequent. When a vein is included in a malignant tumour, carcinoma or sarcoma for example, its wall often gives origin to the morbid tissue which grows in the form of vascular granulations into the lumen of the vessel. These granulations impede the circulation and cause coagulation, so that they may be found inclosed in the substance of a blood clot. Portions of these granulations may also become detached and form emboli. It is probable that the generalisation of certain sarcomata, encephaloid sarcoma particularly, is brought about by the transportation of fragments of the morbid tissue, which are carried away by the blood current and engrafted in various organs, particularly in the lungs, and become the origin of secondary tumours. Also primary tumours of the kidneys, testicles, and limbs become generalised in the lungs, while those which are primarily seated in the stomach and intestine are specially generalised in the liver. In the first case, transportation of the metastatic product is effected by the general venous system, while in the second it occurs through the portal system. The sarcomata seem to be especially diffused by venous metastasis, while the carcinomata give origin to secondary tumours, which almost always develop in the course of the lymphatic vessels.

CHAPTER XII.

LESIONS OF THE LYMPHATIC VESSELS.

I. Normal Histology of the Lymphatic Vessels.

THE structure of the lymphatic trunks and vessels is similar to that of the veins of the same calibre. Three coats, an external adventitious, a middle muscular, and an extremely delicate internal coat lined with endothelial cells, are described, as in the veins. The valves are much more numerous in the lymphatics than in the veins; above the valve the vessel is enlarged, and at this spot the middle coat shows a number of muscular fibres crossing in every direction. In other regions the muscular elements have, on the contrary, a transverse direction. The supra-valvular enlargements seem to play an important part in the circulation of the lymph. The lymphatic capillaries, like the blood capillaries, have no muscular elements; they are seen in the form of cylindrical or flattened tubes lined by characteristic endothelium; the cells composing it show, after being stained with nitrate of silver, blunt lateral teeth, which cog with others on neighbouring cells. While the veins have their origin in capillary networks, the lymphatics originate from the midst of the tissues, and have, at their commencement, no direct communication with the vascular system. The lymphatics empty into the subclavian veins, on the left side by the thoracic duct, and on the right side by the great lymphatic trunk; thus the lymph absorbed directly from the tissues is mixed with the venous blood after having circulated in the lymphatic system. From the discovery of the lymphatics to the time of Magendie an exclusive activity had been attributed to lymphatics in the phenomena of absorption; but though Magendie proved that the veins absorb actively, the lymphatics must still be considered the principal agents of absorption.

One of the most interesting and the most disputed questions is the **origin of the lymphatic vessels** in the tissues. At the time that these vessels were studied by means of injections of mercury under strong pressure, it was thought that the network thus injected was the sole origin of the lymphatic system; but since much more penetrating fluids have been made use of, such as Prussian blue dissolved in water, for example, numerous lymphatic vessels can be injected into which the mercury could not penetrate. It is even sufficient to make an interstitial injection of Prussian blue into the connective tissue for this fluid to penetrate some lymphatic vessels, though the lymphatic reticulum cannot be completely filled in this way. To do so it is necessary for the point of the cannula to be inserted directly into a vessel. It must nevertheless be admitted that the lymphatic vessels open into the meshes of the connective tissue, since on injecting the latter the fluid constantly penetrates into some of the lymphatic vessels. We have already shown how the serous cavities are appendages of the lymphatic system, in that there exist direct communications between them and the lymphatic vessels; hence there can be no pathological change of serous membranes without the corresponding lymphatics being simultaneously altered.

II. Pathological Histology of the Lymphatic Vessels.

Lymphangitis, or **inflammation of the lymphatic vessels**, is a rather frequent affection, being sometimes acute, sometimes chronic, and varying in intensity. It has been particularly studied on the surface of the serous membranes and in the uterus. In pleurisy, pericarditis, and peritonitis, sections passing through the exudation and the subjacent serous membrane show very distinctly the lumina of lymphatic vessels divided in various directions; they are then seen to be dilated, and to contain a substance resembling the exudation on the surface of a serous membrane, and when the inflammation is purulent they contain pus or fibrin inclosing pus cells. Their endothelium is always swollen, desquamated, and proliferating, and their walls are infiltrated with new elements and even with pus cells. In acute lymphangitis of the limbs the suppurative inflammation extends to the cellulo-adipose tissue surrounding the inflamed lymphatics, so that they, together with the indurated tissue, form hard cords infiltrated with pus, and of a much larger diameter than normal full lymphatics. In puerperal metritis the lymphatic vessels, which are found at the angles of the uterus and in the broad ligaments, are often found dilated and filled with pus, and their coats infiltrated with pus cells. The perivascular sheaths of the brain have been regarded as veritable lymphatics; but they are in reality appendages of the subarachnoid spaces. The pathological changes observed in these sheaths will be described when considering the diseases of the encephalon.

It should be added that in certain cases of carcinoma of the stomach, lymphatic vessels are met with in the pleura and lung completely filled and distended with more or less caseous pus. MM. Raynaud, Troisier, etc., have published cases of this kind. We also have observed similar changes of the pulmonary lymphatic vessels in a case of syphilitic gummata of the stomach (for further details see article Lung). This repletion of the lymphatic vessels of the pleura and lung in tumours of the stomach cannot be regarded as resulting from the direct transportation of the products of the primary tumour into the lymphatics. We consider that it should rather be attributed to secondary subacute lymphangitis, which is simply inflammatory in certain cases and of a carcinomatous nature in others, and which is related to the simple or cancerous inflammation of the bronchial glands.

Dilatation of the lymphatic vessels (Lymphangiectasis).—In elephantiasis and congenital macroglossia the lymphatic vessels are dilated without undergoing any notable changes of structure; their epithelial cells are well developed and easily seen. The injection of these vessels is always much easier than when in the normal state (*vide* p. 243).

Lesions of the lymphatic vessels in tumours.—*Tuberculosis* of lymphatic vessels is very often observed in the serous membranes —pleura, pericardium, peritoneum. In the visceral peritoneum, near to tubercular ulcers of the intestine, knotty, white, opaque cords are often seen radiating from the indurated base of the ulcer; these cords, which are raised on the peritoneal surface of the intestine, cross the mesentery to reach the neighbouring lymphatic glands. Upon their surface prominent tubercular granulations are often seen, and on cutting them across a white or yellowish opaque caseous substance can be turned out. In these vessels are found ordinary lymph cells, much larger corpuscles filled with fat granules, and free fat granules. In histological preparations all the phases of development of tubercular granulations may be observed. In the first stage the vessels are filled with cellular elements, some of which are ordinary lymph cells, others very probably derived from the vascular endothelium. The walls of the lymphatics and the neighbouring connective tissue are infiltrated to a great extent with embryonic cells. In the second stage the cells grouped in the wall of the lymphatics and in the connective tissue form nodules, having all the characters of tubercular granulations; these nodules are rather far apart; sometimes, however, they almost touch, and blending with neighbouring granules form a mass of confluent tubercles. Tubercular inflammation of the lymphatic vessels may also be propagated to the thoracic duct, which is often found filled with caseous pus, while tubercular granulations are formed in its wall.

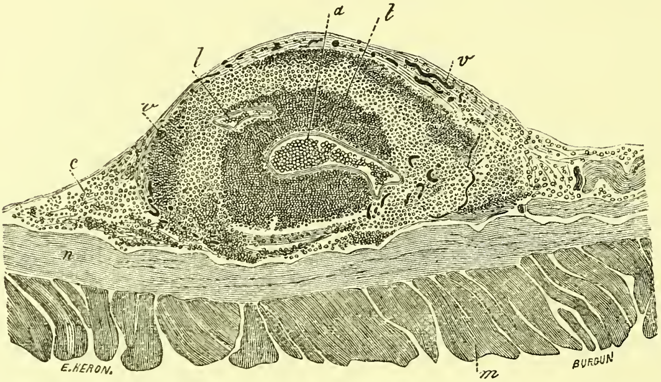

FIG. 255.—TRANSVERSE SECTION OF A TUCERCULAR LYMPHATIC VESSEL ON THE SURFACE OF THE INTESTINE.

a, cavity of the lymphatic vessel, which is seen to have undergone contraction and to be filled with lymph cells; *c*, sub-peritoneal connective tissue, in the midst of which passes the lymphatic vessel, the walls of which are much thickened by the development of tubercular tissue; *l*, tubercular tissue, the external zone of which is formed of round cells much larger than those of the internal zone which are caseous; *v*, capillary vessels; *n*, layer of longitudinal smooth muscle cells; *m*, layer of transverse muscle cells of the intestine.

When **carcinoma** produces inflammation in the lymphatic vessels which pass from the tumour, they form hard cords, gradually increasing in size until they reach that of a crow's quill. This may occur in certain hard carcinomata of the mamma, in which many repeated attacks of angioleucitis terminate by transforming the lymphatic vessels into hard full cords, entirely scirrhous in structure. In secondary carcinomata of the lungs and pleura, knotted networks of grey, indurated, semi-transparent or opaque lymphatic vessels are sometimes seen upon the surface of the serous membrane. The vessels composing these networks contain a milky juice, formed of large cells resembling those of the tumour. Small carcinomatous nodules are often found in their walls. The same carcinomatous degeneration of lymphatic vessels may be observed in other serous membranes, particularly in the peritoneum. Lymphatics communicate with the alveoli of carcinoma (p. 179), and it is hence very probable that the carcinoma cells they contain penetrate into these vessels, and are carried for a variable distance; they then undergo multiplication and become the starting-point of carcinomatous change in the walls of the lymphatics, and of secondary nodules in their neighbourhood.

CHAPTER XIII.

LESIONS OF THE LYMPHATIC GLANDS.

I. Normal Histology of the Lymphatic Glands.

FROM the descriptions given by various authors, it might be thought that the structure of lymphatic glands is very complicated, but it is in reality extremely simple. A lymphatic gland presents for consideration a fibrous capsule, a cortical substance, which is interrupted only at the hilus, and which contains the follicles and the sinuses, and, finally, a medullary substance which extends as far as the hilus, and which contains the follicular cords and cavernous lymphatic spaces.

In the fibrous capsule the connective-tissue fasciculi form a kind of felting, much more closely woven than ordinary loose connective tissue. From this capsule spring fibrous trabeculæ, which divide, anastomose, and finally converge towards the hilus of the gland where they terminate. The capsule is traversed by afferent lymphatic vessels at different points on its surface, the hilus excepted, and they open into a cavernous system, the arrangement of which will be described later. The efferent vessels also originate in this cavernous system, and may be recognised as distinct canals in the hilus of the organ at which they issue.

The **cavernous system,** which corresponds to the lymphatic sinuses and channels of His, is permeated by the arteries and veins of the gland. These blood-vessels are not only found in the spaces of this system but in the centre of the fibrous trabeculæ, which are derived from the capsule and converge towards the hilus. From these fibrous trabeculæ spring small fasciculi of connective tissue, which, dividing and anastomosing with neighbouring fasciculi, form a complicated network, which, from the histological point of view, does not essentially differ from the structure of the great omentum, excepting that these trabeculæ radiate in every direction, while in the great omentum they are placed in the same plane. In sections of glands cut perpendicularly to an artery the artery is seen to be surrounded by a ring, which represents a transverse section of a fibrous trabecular septum; from the margin of this ring spring radiating fasciculi of retiform connective tissue. These trabeculæ have no nuclei either within them nor along their tract, nor at the points where they intersect; they are covered with flat endothelial cells similar to those observed on the fine trabeculæ of the great omentum. The meshes of this reticulum of the cavernous system are filled with lymph which is extremely rich in cells; thus, in order to examine the structure of a lymphatic gland, the cells must be removed with a camel's-hair brush.

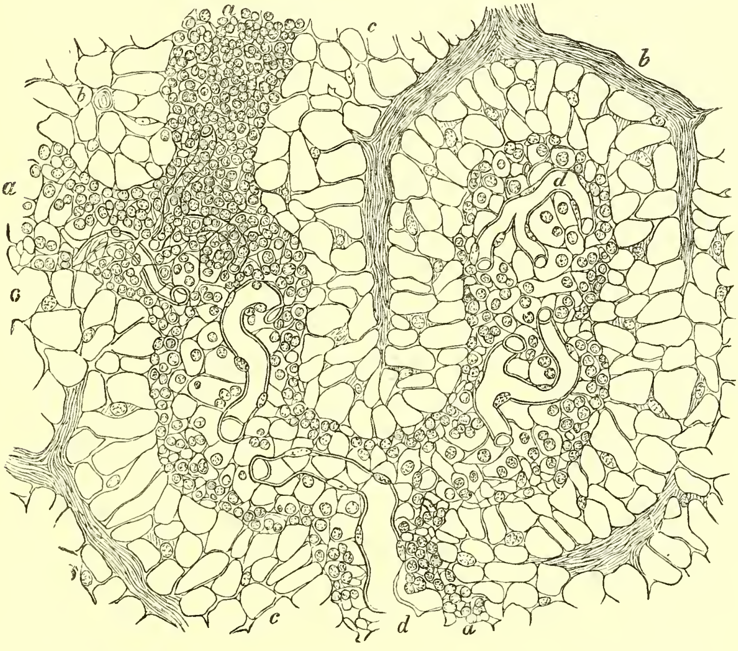

Fig. 256.—Section of the Medullary Tissue of a Lymphatic Gland of the Ox.

a, follicular substance; *b*, fibrous septa; *c*, lymph channels; *d*, capillary blood-vessels. Magnified 300 diameters. (Figure borrowed from Recklinghausen.)

If a lymphatic gland be injected with a solution of Prussian blue, the coloured fluid fills all the system of lymphatic channels, and returns by the efferent vessels. In sections of a gland thus injected it will be seen that the injection has not found its way into all parts of the gland; it has only penetrated into the channels filled with lymph from the afferent to the efferent vessels, marking out, in the cortical substance, the lymph sinuses, and in the medullary substance the cavernous spaces which lead to the efferent vessels; but it has left the follicles and follicular cords entirely unstained.

The **follicles** are best seen in the glands of the mesentery at the moment of digestion, for they are then slightly translucent, while the lymphatic channels described above are filled with chyle and form opaque sinuses. These follicles are round upon the free surface of the gland, while at the hilus they form one or more sinuous and characteristic prolongations, to which the distinctive name of **follicular cords** has been given. We designate the entire follicle by the name of the **follicular system,** reserving to the channels through which the lymph circulates the name of **the cavernous lymphatic system.** The arteries and veins of the gland contained in the great fibrous trabeculæ ramify in the cavernous spaces, while the blood capillaries are only found in the follicular system, where they form a network.

The tissue composing the follicles and follicular cords is similar to that present in the whole cavernous system; it differs from it only by the extreme thinness of its trabeculæ, and by the smaller size of its meshes. The capillaries which ramify in the follicular substance are surrounded by a special layer of fine fibrils, which divide and anastomose, and finally blend with the trabeculæ of the connective-tissue reticulum of the follicular substance. There are neither nuclei nor cells in the substance of these trabeculæ, nor at their points of intersection. The nuclei, described by some authors, belong to the extremely delicate endothelial cells which line the surface of the trabeculæ of the reticulum, covering them like a varnish.[1]

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[1] To be convinced that the nuclei observed on the trabeculæ of the reticulum of the follicular substance, as well as of the cavernous system, are not contained within the trabeculæ, recourse must be had to the following methods. Two similar lymphatic glands are removed from a dog which has just been killed; into one of them a cubic centimetre of a 1 per cent. solution of osmic acid is injected; the gland is then hardened by submitting it to the successive action of alcohol, and gum and alcohol, and sections are cut from which the cells are brushed away. Along the trabeculæ, and at their points of intersection, distinct oval nuclei will be recognised. The other gland is placed for twenty-four hours in a 33 per cent. solution of alcohol, and is then hardened with gum and alcohol. The sections cut are immersed in water, brushed with a camel's-hair brush, when the reticulum of the reticulated substance, as well as the cavernous system, is seen to be entirely deprived of any cellular elements. Two different preparations are thus made, showing the structure of the reticulum; in one all the nuclei are preserved, in the other all the nuclei have disappeared; in the first preparation, the endothelial cellular elements acted upon by the osmic acid have been fixed; in the other they have, on the contrary, been removed from the trabeculæ by the

The limit between the follicles and the cavernous lymphatic system is tolerably distinctly seen in preparations made after the interstitial injection of Prussian blue, or in preparations hardened with alcohol, and from which the cells have been washed away with a camel's-hair brush. In the cavernous tissue the meshes of the reticulum being larger and the lymph cells less numerous than in the follicular system, they are easily removed, and the cavernous system is seen to form so many clear spaces, but no true limiting membrane can be distinguished between the two systems; it may in fact be proved by experiment that there is easy communication between them. To demonstrate this fact, fine powdered vermilion suspended in water is injected into the deep connective tissue surrounding the sciatic nerve of a rabbit. The animal being killed forty-eight hours afterwards, the lymphatic vessels proceeding from the region where the vermilion had been introduced are found filled with it, as if they themselves had been injected. The lumbar glands, to which these vessels pass, also contain vermilion, which is found particularly in the cavernous system, so that on the surface of the organ the follicles appear as white circles surrounded with red bands. In sections made after hardening, it is seen that the particles of vermilion are contained in the cells, namely in the lymph cells and in the endothelial cells lining the trabeculæ of the reticulum; but particles of vermilion may also be observed in a few of the lymph cells of the follicular substance.

In the physiological phenomenon of the transportation of the chyle through the mesenteric glands during digestion, fat granules are found, not only in the spaces of the cavernous lymphatic system, but also, though in smaller numbers, in the cells of the follicular system. It is hence probable that the meshes of the retiform tissue of the follicles are in communication with the meshes of the cavernous system, from which it may be concluded that a lymphatic gland is nothing more than a complicated lymphatic cavity, or a serous cavity placed along the course of lymphatic vessels. The afferent vessels enter this cavity at different points on the surface of the lymphatic gland, and the efferent vessels issue from it at the hilum; they are here side by side with arteries and veins which have distinct walls, while the efferent lymphatics

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action of the dilute alcohol, which acts as a dissociating fluid. It may hence be concluded that nuclei existed on the surface of the trabeculæ, and that they were removed by the camel's-hair brush, which would not have affected them if the nuclei were located in the substance of the trabeculæ.

are simply canals hollowed in the substance of the connective tissue and lined with an endothelium.

If circulation of the lymph is easy in the cavernous system it is not the case in the follicular system. It is probable that the parts composing it, the follicles and follicular cords, play an important part in the formation of the lymph cells, which after being developed in the follicular substance penetrate into the cavernous system, and thus enter the great lymphatic circulation.

II. Pathological Histology of the Lymphatic Glands.

Pigmentation of glands.—The peri-bronchial lymphatic glands of adults and old persons may be often seen to be of a black colour. A similar pigmentation may be seen in other glands, when the regions from which their afferent vessels are derived have been the seat of infiltration of blood or foreign granular and coloured substances. Thus in tattooing, the coloured powders introduced into the skin are subsequently found in the corresponding lymphatic glands. If the coloured particles, instead of being deposited in the connective tissue, existed or were introduced into the blood, pigmentation of the lymphatic glands would not occur or would be very limited; this fact results from the experiment of Langerhans. It has already been described with what rapidity coloured particles penetrate the lymphatic glands when deposited in the connective tissue; it has also been seen that when extravasated blood undergoes a series of metamorphoses ending in the formation of pigment granules, they are taken up by the lymphatics and become fixed in the glands. Thus, the coloured particles found in glands are of two kinds—they are either derived from the blood, or they are foreign to the organism; the former are yellowish-red, brown or black, round or angular, some observers having also found alongside them true crystals of hæmatoidin (Rebsamen); the latter, formed of opaque substances, always appear black or dark to transmitted light, and may be carbon, vermilion, metallic powders, etc. Glands infiltrated with pigment are of a grey slate colour, black, or marbled grey, white and black. The pigmentation is particularly seen in the cavernous lymphatic system, the follicular system being very faintly coloured. If there are a few blackish striæ, they exclusively occupy the spaces of the cavernous system.

Glands infiltrated with pigment are generally larger and firmer than normally. The increase in size of a gland by penetration of pigment may be easily reproduced in experiments on animals. If half a cubic centimetre of water holding particles of vermilion in suspension be injected into the peri-sciatic tissue of the rat, one of the two lumbar glands deeply stained by the vermilion will, at the end of twenty-four hours, be found twice as large as the corresponding gland. This increase in size is not solely due to accumulation of foreign particles, but chiefly to the congestion and inflammation they have caused.

In man certain pigmented glands are hard, and show on section a hard spiny surface, from which no juice can be pressed. The slow irritation caused by the presence of the pigment has produced a true fibrous change. In sections it will be seen that the arteries are surrounded with thickened fibrous zones, and that the connective tissue cells are infiltrated with pigment; the trabeculæ of the reticulum of the cavernous substance are hypertrophied, and their endothelial cells contain pigment granules; the lymph cells which crowd the meshes of the reticulum also contain them. The follicular substance is no longer distinct from the cavernous system, the retiform tissue may even have entirely disappeared, and the perivascular connective tissue, infiltrated with pigment, may fill up the whole organ. But these examples of complete transformation of the glands, and interstitial adenitis with pigmentation, are only found in old persons or in miners. Glands which are only slightly pigmented, as, for example, the bronchial glands after pneumonia, the glands of the articular folds after phlegmon or hæmorrhage into the connective tissue of the limbs, show very different appearances. They are hypertrophied, and yield a very abundant juice, in which are found small, spherical cells containing yellowish-red or brown pigment granules, also large stellate or angular cells, containing many oval nuclei and pigment granules. When the change is old, all the pigment granules are absolutely black. On dividing the glands it is seen that the cavernous substance is principally the seat of pigmentation, and that side by side with pigmented lymph cells there are others which are colourless. The endothelial cells of the reticulum of the follicular substance also contain coloured granules; they are then slightly tumefied and can be more easily detached.

Acute adenitis.—Inflamed glands are sometimes considerably increased in size; they then tend to take a spherical form, or if in contact with neighbouring glands equally tumefied they become flattened one against the other. The surrounding connective tissue is the seat of inflammatory œdema, the blood-vessels are dilated, and around them small ecchymoses are found. In acute adenitis this œdematous connective tissue shows purulent foci, or even abscesses may be formed, so that the lymphatic gland may be entirely surrounded with a layer of pus; this lesion has been called peri-adenitis. In the gland itself are found lesions which vary according to the degree of the inflammation. In the first stage there is inflammatory œdema, which is particularly well marked; in the cavernous lymphatic system the follicles and follicular cords are much more distinct than usual, and they form dark spots or lines on a slightly transparent groundwork. In some cases, the hyperæmia and effusion of blood which accompany adenitis cause, with increase of volume, a red or reddish-brown pigmentation of the entire gland, which then resembles splenic tissue. Such is the lesion generally observed in the bronchial glands after pneumonia or acute capillary bronchitis. The juice of these glands contains, besides ordinary lymph cells, other lymph cells in which red blood corpuscles or fragments of them are found. A great number of red corpuscles also float in the fluid of the preparation. At a more advanced period the distinction between the two systems of the gland is no longer possible, and on scraping the divided surface a very abundant juice is obtained, as in soft carcinoma. In section of a normal gland, twenty-four hours after death, a slightly milky fluid is obtained similar to that yielded by encephaloid sarcoma, but in inflammation this juice is much more abundant and more milky. Examined under the microscope this juice is seen to contain a large number of lymph cells, and large tumefied endothelial cells containing one or more nuclei; sometimes the latter, which may reach a diameter of ·03 mm., resemble the multi-nucleated cells of bone medulla; they are smaller, and contain fewer nuclei than those found in certain forms of subacute or chronic inflammation, to be studied further on.

In diffuse suppuration of glands their divided surface yields, on scraping, creamy pus, the afferent and efferent lymphatic vessels being filled and distended with the same fluid. Suppurative inflammation of glands may extend to the formation of distinct purulent foci, or to complete purulent infiltration; it is sometimes accompanied with more or less extensive hæmorrhage, the blood infiltrating into the parenchyma of the inflamed gland. The pus cells which fill the purulent foci do not differ greatly from normal lymph cells; they contain, however, a much larger number of fat granules, and beside them may be seen large granular bodies.

In sections of an inflamed gland in the first stage of inflammation, that of swelling and œdema, cut after hardening in picric acid and removal of the cells by brushing, the modifications of cells already described are seen, notably swelling and multiplication of the nuclei of the endothelium. The trabeculæ of the cavernous system are tumefied, and instead of being formed of a homogeneous substance they seem to be composed of a fibrillar and granular substance; they may even attain five or even ten times their normal diameter. In the follicular substance the trabeculæ of the retiform stroma are less swollen, and seem simply strewn with granules.

When the inflamed gland is of a red colour like the spleen, the capillaries of the follicular substance are found to be largely dilated and filled with red blood corpuscles, and between the lymph elements, which crowd the meshes of the retiform stroma, collections of red blood corpuscles may be observed, or are regularly disseminated. To accurately observe this change the gland should be hardened in alcohol, delicate sections cut, stained with carmine and mounted in glycerine; the red blood corpuscles will then be seen as small clearly defined rings, unstained by the carmine. When the adenitis is purulent, irregular loss of substance may, in microscopical sections, be observed near the purulent foci, and at their margins the process of destruction of the fibrils of the retiform stroma may be followed. These fibrils are seen to swell, soften, and finally break down into a granular detritus, which is absorbed by the neighbouring lymph cells. It will also be observed that the loose connective tissue around the large vessels is infiltrated with pus cells.

Acute adenitis is rarely primary; it is most frequently observed in glands of which the lymphatic radicles originate in an inflammatory focus. It is thus very probable that inflammation of the gland is related to absorption of irritating substances—still ill determined—which are elaborated in the inflammatory focus, or derived from the exterior. As examples of inflammatory foci causing adenitis, we may mention pneumonia, bronchitis, impetiginous eczema, chancre, blennorrhagia, excoriations and ulcerations, ulcerations of the intestine, especially those of typhoid fever. Adenitis may also be observed in infectious diseases—syphilis, plague, scarlatina, variola, etc.—in which there is most probably transportation of the virulent matter by the lymphatic channels.

Chronic adenitis.—Simple fibrous degeneration, simple or scrofulous caseous degeneration, and, finally, calcareous degeneration of lymphatic glands, are generally referred to chronic inflammation.

Fibrous induration is rather common in the bronchial and inguinal glands of persons advanced in age ; it is most frequently accompanied with slight hypertrophy and pigmentation; it consists in an increase in thickness of the perivascular connective tissue of the cavernous system; the reticulated trabeculæ of this system may become double or triple their normal size, and at numbers of points they appear to be fibrillated. The follicular parenchyma appears, on the other hand, to be more or less considerably atrophied, and may even entirely disappear ; generally, only a few disseminated, irregularly shaped fragments are found, particularly towards the periphery of the gland.

In lymphatic or *scrofulous* subjects, enlargement of the glands generally follows catarrhal inflammation of the mucous membrane, or moist eruptions of the skin, and ends in the degeneration of glands, which were previously hypertrophied. Hypertrophied and strumous cervical glands are frequently discovered after death or after surgical operations. They are generally united into one large mass; in the same individual they may have very various appearances, some being in an advanced morbid condition, while others show all the different phases of evolution of scrofulous adenitis ; some are simply hypertrophied and congested, others show the characteristic appearances of scrofulous adenitis fully established. The shape of the glands is preserved, though they are extremely large, of a pale grey yellowish colour, and soft elastic consistence. Their surface on section is generally dry, and, on looking attentively with a magnifying glass, a crowd of small grains or opaque points on a grey semi-transparent base is perceived. These small opaque points form by their growth and union small yellowish caseous foci, more or less resistant. In a later stage these foci are fused together, and form an opaque whitish grumous mass, varying in firmness and dryness according to the age of the lesion. When this degeneration is old the hypertrophied gland seems to be composed of a chalky, dry, non-vascular substance, which breaks up into grumous fragments, and is enveloped by the thickened capsule of the gland. Calcareous degeneration occurs as the final stage of this lesion. In old persons, glands are rather frequently found formed of a fibrous capsule, containing a slightly lobulated calculus, held to the capsule by fibrous filaments which penetrate into its interior. This calculus is friable, or is sufficiently firm to rebound if let fall on a hard surface. It is rare, however, for petrifaction to be so complete, for petrified glands generally only contain one or more calcareous masses varying in size and shape.

On examining **strumous glands** under the microscope, at the period when they are hypertrophied, yellowish-grey in colour, and sprinkled over with small points or opaque foci, two lesions are found: thickening of the fibrous trabeculæ, and granulo-fatty degeneration of the cellular elements of the follicular system. Quite at the commencement, the fibrous tracts which pass from the periphery of the gland towards the hilum are thickened, and form bands of connective tissue which accompany the blood-vessels, and divide the adenoid tissue into distinct islets. As the connective tissue becomes more abundant the islets of adenoid tissue, which it surrounds, take a spherical form. Here the same phenomenon occurs as in certain forms of cirrhosis of the liver, in which the hepatic lobule is divided and subdivided into small groups of round cells, surrounded by bands of fibrous tissue. Sections, stained with picrocarminate of ammonia and examined under a low power, show small islets stained orange-red, formed of the retiform tissue of the follicles, and surrounded by broad bands of embryonic or fibrous connective tissue stained red by the carmine; in these islets are found large cells, containing one large ovoid nucleus with a nucleolus, and formed of a delicate, soft, granular protoplasm, often including fat granules. These cells, the nucleus of which stains easily with carmine, are elongated, slightly flattened, or globular; they rarely contain two nuclei. The structure of these foci can be better studied in sections cut as fine as is possible in the fresh state, and from which the lymph cells have been removed by a camel's-hair brush, and afterwards stained with picrocarminate. They are then seen to be composed of a reticulum, the fibrils of which are softer, thicker, and more granular and friable than the normal fibres of the follicular retiform tissue. When examined under a very high power, small granules are seen on the margins of these fibrils, and their surface is rough; they are infiltrated, tumefied, and softened; the meshes which they form are much larger than normally, and inclose large granulo-fatty cells with ovoid nuclei, just described. At the points where the cells have been altogether washed away by the camel's-hair brush a few fatty granules still remain, fixed to the fibrils of the reticulum.

In sections made after the gland has been immersed for some time in dilute alcohol, and from which the cells have been washed away by agitation of the section in water, a clear space is seen with the naked eye in the place of the formerly dark spot, and is found under the microscope to be the framework of retiform tissue with its capillary vessels. The fibrous tissue surrounding the opaque spots is formed of fibrils belonging to the primary retiform tissue, but thickened and rigid; they run in a direction parallel to the surface of the small foci, and contain small round cells between them. In sections obtained after complete hardening in Müller's fluid, or in gum and alcohol, the islets and the bands of fibrous tissue which separate them are well seen; the fibrous capsule of the gland is also seen to be thickened, but the retiform tissue of the islets cannot be cleared by means of a camel's-hair brush. When the caseous islets are older, the vessels crossing them are obliterated, and in transverse sections, made at right angles to their axes, they are seen as so many circles filled with nuclei, and resemble giant cells. The cells contained in the reticulum then become more and more granular, and finally atrophy. The caseous islets become more or less completely separated from the tissue which surrounds them, and seem to be limited by septa.

In consequence of the confluence of the caseous islets, or of the caseation of a group of islets and the connective tissue surrounding them, the gland becomes yellow and friable for a more or less considerable extent. The caseous parts are almost always spherical, and surrounded by a fibrous membrane; in them are only seen round atrophied cells, slightly transparent or granular, lying in contact with one another. The fibrous tissue is dense, homogeneous, and semi-transparent, and is united to the thickened capsule of the gland. The surrounding cellulo-adipose tissue has disappeared, and is replaced by sclerotic tissue which is often closely united to neighbouring parts, to the submaxillary or parotid glands, for example. This change, which differs in a marked degree from tubercle, properly so called, of the lymphatic glands, is of the same order as the caseous changes which occur in other organs in scrofulous subjects. It is possible that in certain cases it is related to tuberculosis, for, as we have already said (p. 201), this disease may manifest itself, not only by characteristic tubercles, but also by inflammation which has a tendency to terminate in caseous degeneration; in the same way as syphilis is shown simultaneously by gummata, and by various inflammatory neoplasms ending in caseous degeneration, and which differ essentially from those of tuberculosis by the tendency they show to form connective and osseous tissue.

The **stony masses** of the lymphatic glands do not possess the structure of bone; examined in delicate sections they are seen to be transparent, and to contain irregular fissures, and striæ; they are partly soluble in hydrochloric acid, when they give off carbonic acid gas.

Amyloid degeneration of lymphatic glands.—This lesion is met with in connection with similar changes in the spleen, kidneys, and liver under the same circumstances, that is to say, in cachexia due to suppuration of long standing. It is accompanied with a regular hypertrophy of the gland, which may be sometimes very marked. On dividing the gland, grey semi-transparent spots will be seen either throughout its whole extent or in its cortical substance, which spots become of a mahogany-red colour when treated with a solution of iodine, and sometimes violet, bluish, and green bands appear on adding sulphuric acid to the parts already stained by the iodine. The lymph cells are infiltrated with amyloid substance, and are transformed into small, transparent, and homogeneous blocks, made angular by reciprocal pressure. The capillaries and arterioles have equally undergone amyloid degeneration and show the appearances already described on pages 517 and 525. The amyloid lesion is limited to the follicles of the cortical substance and follicular cords, to the exclusion of the cavernous substance and lymph channels. In delicate sections, made after hardening in alcohol, and staining with Paris violet, amyloid degeneration of the retiform tissue of the follicles may be recognised. In much hypertrophied glands, the anatomical signs of chronic inflammation may also be observed. The lymph channels and sinuses are very much enlarged and filled with spherical cells, containing one or more nuclei; at the same time the endothelial cells lining the walls of the lymph channels and their septa are tumefied and granular, and show multiplication of their nuclei. The connective tissue of the gland may also be thickened.

Colloid change.—We have frequently met with a lesion of lymphatic glands, consisting in colloid degeneration, the cause of which we were unable to discover. In sections cut after hardening in alcohol, the degenerated parts are seen to be formed of a series of alveoli of various sizes, filled with a colloid and refractive substance. These alveoli are separated by fibrous trabeculæ, on the margin of which are often seen rows of spherical cells, some of which are vesicular and contain colloid matter. This morbid change is without clinical interest; it is particularly seen in subjects advanced in age, and seems to be related to an arrest of the function of the gland.

Tumours of the lymphatic glands.—Almost all tumours of the lymphatic glands, with the exception of hypertrophy due to leukæmia or œdema (*vide* pp. 248 and 465), are secondary. It may be said, in a general way, that all glandular tumours resulting from a primary tumour, such as sarcoma, carcinoma, tubercle, chondroma, epithelioma, etc., faithfully reproduce the anatomical form and structure of the primary tumour with which they are connected by their afferent lymph vessels. The glands affected in the vicinity of the tumour sometimes even better enable us to determine the nature of a tumour than examination of the primary tumour itself: if, for example, an ulcerated and gangrenous tumour of the cervix uteri is under examination, study of the glands of the lower pelvis, secondarily affected, would serve better to determine the nature of the neoplasm than examination of the organ primarily affected.

Sarcoma is much rarer in the lymphatic glands than carcinoma and epithelioma. We have already seen, in fact, that carcinoma and epithelioma are particularly propagated by lymph vessels, while sarcoma becomes generalised by the circulation. If, however, sarcoma is developed in the vicinity of lymphatic glands, they may be affected by extension of the tumour, in which case the capsule and parenchyma of the gland are seen to be successively changed into sarcomatous tissue.

A species of tumour, called by Billroth **adeno-sarcoma,** is on the contrary generalised by means of the lymph channels. It is difficult to fix the place adeno-sarcoma should occupy in the classification of tumours; it may be only a variety of carcinoma. It causes the successive transformation of a chain of glands, a change characterised by considerable hypertrophy of the glands affected. These glands, which are quite encephaloid in appearance, are often fused with neighbouring glands into a single mass; they yield an abundant juice, in which large cells of various shapes, and containing large nuclei, may be seen. In sections cut after hardening, fibrous trabeculæ are recognised, and from them springs a large-meshed fibrillar reticulum, the fibrils of which are covered with flat cells, these meshes containing the polymorphous and voluminous cells spoken of above.

Carcinoma of the lymphatic glands is very common; thus carcinóma of the mamma is almost always complicated with what is called induration of the axillary glands. Some of these glands are small, firm, and fibrous in appearance, others are composed of a tissue resembling that of the primary tumour. We have already seen, on page 179, that fibrous degeneration of the lymphatic glands often precedes the formation of characteristic carcinomatous tissue. Fibrous change is brought about by a very simple histological process. All the fibrils of the reticulum, in the cavernous as well as in the follicular system of the gland, hypertrophy so that the alveoli between them become smaller and smaller, and sometimes even entirely disappear. In this way the lymph channels of the gland may become almost entirely obliterated. The gland thus altered is, for a certain time, a barrier to the propagation of cancer; but after having undergone this remarkable fibrous alteration it shows later on the characters of carcinoma, and becomes itself a new focus of infection. When secondary carcinoma of the lymphatic glands develops rapidly, the cellular elements contained in the trabeculæ of the reticulum take at once the form of the so-called cancer cells, while the trabeculæ gradually increase in thickness, to form the septa of carcinomatous tissue. Regarding the formation of cancerous alveoli in fibrous tissue (*see* p. 176), we have already shown that when lymph vessels proceed from a cancerous tumour, they contain large polymorphous cells; the afferent vessels of lymph glands undergoing cancerous degeneration often also contain similar cells; it may hence be supposed that infection is produced by the transportation and grafting of cancer cells, or that these cells having once reached the gland are the starting-point of the change.

Tubercle of the lymphatic glands.—Tuberculosis of the lymphatic glands is very common: the glands of an organ affected with tuberculosis, as the lung or intestine, almost always show tubercular granulations. We recommend the mesenteric glands for this study, for they are not encumbered with coloured particles like the bronchial glands. In tubercular ulceration of the intestines, if the lymph vessels, which are generally inflamed and tubercular, are traced from the intestine to the lymphatic glands of the mesentery, the latter will almost invariably be found to be tubercular. Tubercular granulations are often observed on the surface of the glands, in the fibrous capsule itself, and sometimes round the afferent vessels, where they have the same relations as in other lymph vessels, such as on the surface of the peritoneum, for example (*vide* p. 540 and fig. 255).

Tubercular glands vary greatly in size; they are often small, hardly larger than normal, though they may contain one or more discrete granulations, or even groups of confluent granulations. The size is more particularly related to the various processes of inflammation which complicate tubercle. Thus at the beginning, granulations are accompanied with intense inflammatory congestion, when it is not rare for the glands to attain a very large size; their surface on division is thin, red, and saturated with a milky fluid more or less blood-stained. Tubercular glands of the mesentery are sometimes infiltrated with pus, in which case they become still larger.

On examining, with the unaided eye, a tubercular gland which has been divided in its long diameter, the granulations cannot always be seen, the surface only looking a little drier than normally without change of colour; it is rare for the granulations to make marked prominences in section; they are more frequently seen in the form of grey or yellowish-grey spots, more opaque and drier than the rest of the section. Such an appearance, however, signifies that the granulations are confluent. When they are older they are yellow and caseous. Sometimes, in glands near the bile duct, the tubercles are seen to be of a bright yellow colour, which is due to the fact that they are infiltrated with the colouring matter of the bile. We once had occasion to see tubercles in the bronchial and cervical glands stained with bile.

Sections of glands, containing a small number of recent granulations, show that they are most frequently located in the retiform tissue of the follicles near to the capsule. In shape they are more or less regularly circular, of a diameter of ·05 to ·10 mm., and by the fusion of many together they may extend and form irregular masses. The blood-vessels surrounding them are very much dilated. The granulations are composed, at their commencement, of retiform tissue, in which the lymph cells seem to be heaped together, and to have become granular and atrophied; the capillary blood-vessels are soon obliterated and giant cells are formed. The retiform tissue near the granulations is continued into their interior, they not differing from normal retiform tissue except by some slight modifications of the lymph cells and capillaries they contain. In granulations the lymph cells are atrophied and pressed together, and the fibrils of the retiform tissue become thinner and granular, till the reticulated stroma and the cells are closely united, and the whole tissue, with numerous giant-cells scattered through it, ultimately undergoes caseous degeneration.

The development of tubercular granulations is almost always accompanied with more or less acute inflammation; the sinuses and the whole cavernous system are then filled and distended with large granular cells, containing one or more oval nuclei and sometimes red corpuscles; these cells are derived from the endothelial or lymph cells. This inflammation of the sinuses and cavernous substance is, when intense and general, shown by hypertrophy of the gland, which on section is seen to be pinkish or grey, and saturated with a milky and blood-stained juice. Small colloid spots are sometimes seen in the cortical substance, or in the midst of the follicular tissue of inflamed and tubercular glands; these spots are formed of masses of clear, transparent, non-nucleated lymph cells, with colloid contents, and are two or three times larger than normally; they stain with picro-carminate of ammonia, and they give none of the usual reactions of amyloid substance.

Another inflammatory lesion, namely **fibrous degeneration of the retiform tissue**, is frequently observed in tubercular lymphatic glands. The fasciculi of the newly formed connective tissue are thick and homogeneous, and resemble those of the skin; they stain red with picro-carminate of ammonia; they are at first found round the small arteries, and they follow the capillaries and reach the retiform tissue. On dividing a gland this new fibrous formation is plainly seen in the form of small, clear, transparent islets, which stain easily with carminate of ammonia. This chronic interstitial inflammation is even met with in tubercular glands which have undergone suppuration; in fact, suppuration of tubercular glands is not rare; it is observed when tubercles of the organ primarily affected, the intestine or lung, are themselves rapidly destroyed by suppuration, as when, for example, there are numerous tubercular ulcers of the intestine, trachea, or bronchi undergoing rapid destruction, or freely suppurating pulmonary cavities. In such cases one or more glands may be found at the root of a bronchus in a state of suppuration, communicating by a fistulous tract with a purulent focus.

Tubercular granulations finally undergo **caseous degeneration,** which may affect a part or the whole of the gland, which then presents entirely the same appearance as a scrofulous gland in the stage of caseous degeneration. But though termination by caseous degeneration is identical in tuberculosis and scrofula, the initial lesions are very different; at the commencement of tuberculosis, inflammation, characterised by the accumulation of large cells in the lymph sinuses, is observed between the granulations; at the commencement of scrofula, generalised interstitial adenitis is produced, and the small islets already described, which must not however be confounded with tubercular granulations.

Syphilis may cause inflammatory hypertrophy of the lymphatic glands, ending in caseous degeneration. Among syphilitic adenites should be distinguished those which occur at the commencement of the disease simultaneously with chancre and which are continuous throughout the secondary period, and those which show themselves in the tertiary period. On scraping the surface of a divided gland, affected with adenitis **in the secondary period of syphilis**, there are found, first, normal lymph cells; secondly, much larger cells, with an ovoid nucleus; thirdly, large mother-cells, containing one large ovoid nucleus and many other nuclei, generally round. These large cells have a granular protoplasm, are of different shapes, and often contain red blood corpuscles. They are found in the peri-follicular sinuses. The fibrous trabecula of these glands are often thickened when the lesion is no longer recent. Syphilitic cervical glands of young subjects may attain an extraordinary size, and persist for years; they have all the gross and microscopic appearances of strumous glands; we have examined some showing the lesions of interstitial adenitis, and which had at the same time undergone caseous degeneration.

The condition of the lymphatic glands **in the tertiary period of syphilis** is extremely variable; they may be cirrhotic, caseous, or tumefied, of a whitish colour and yielding a milky juice on division. The tumefaction gives the glands a medullary appearance, which has been described by Virchow, who was, however, content with gross appearances. We have made a microscopical examination of a case in which gummata of the stomach and liver were simultaneously present. (‘Mém. de la Société Médicale des Hôpitaux,’ 1874.) All the lymphatic glands situated in front of the cœliac axis, on the superior margin of the pancreas, in the vicinity of the pylorus, and round the bronchi, were white, tumefied, and hard, and from their divided surfaces a few drops of puriform fluid could be squeezed out. This fluid contained, together with round and granular lymph cells, a great number of large swollen endothelial cells, containing one oval nucleus or many nuclei. These glands, hardened by the successive action of Muller's fluid and gum and alcohol, and examined in delicate sections, showed all the circum-glandular and capsular lymph vessels, the lymph channels and sinuses, and all the cavernous tissue, filled and distended by large globular epitheloid cells, derived from the lymph cells and endothelial cells lining the lymphatic cavities and channels. On washing away the cells with a camel's-hair brush, large alveolar cavities, representing sections of afferent lymph vessels, were seen at the centre of the glands; the meshes of the retiform tissue of the cavernous substance were also much enlarged. Wherever an islet of fine retiform tissue was discovered in a section, around it were seen the large meshes of cavernous tissue and the lymph sinuses and channels distended commensurately; these cavities had, however, partly lost their contents, and showed at places large swollen granular endothelial cells, containing one or more ovoid nuclei; these cells were elongated or flattened, and had angular prolongations; sometimes they were of a regular pavement-shape with blunt edges, a shape due to their being flattened by reciprocal pressure. Here, then, was produced an inflammation of all the lymph channels of the gland, an inflammation consecutive to that of the afferent lymph vessels, and originating in the syphilitic lesions of the liver and stomach.

Chondroma of the lymphatic glands is rare, and is chiefly caused by extension of a neighbouring chondroma.

Epithelioma.—Every variety of epithelioma may be met with in the lymphatic glands. In development it differs from carcinoma, in that the first epithelial nodule commences in the cavernous lymphatic system, while the structure of the gland is still preserved; it sends out in various directions buds, surrounded with embryonic tissue, always of the same structure as the primary tumour. Thus in pavement epithelioma with epidermic globes, the glands are transformed into a series of large branching cavities, which are filled with crenated cells, and showing epidermic globes here and there. In cylindrical-celled epithelioma cavities are produced, which are separated by delicate septa lined with cylindrical cells, and filled with a semi-fluid mass containing cellular elements. From the fibrous walls of these cavities often spring vascular fibrous processes, also lined with cylindrical cells.

CHAPTER XIV.

LESIONS OF THE NERVES.

I. Normal Histology of the Nerves.

MEDULLATED nerve tubes and non-medullated, or Remak's, fibres (already described on p. 31) form nervous fasciculi, varying in diameter; one of these fasciculi may alone constitute a nerve, but they are more frequently associated in varying numbers. In man the large nerves of the limbs contain a great number of fasciculi. Each nervous fasciculus is surrounded by a sheath, which in the terminal branches is formed of a single layer, and which we call the sheath of Henle; in much larger fasciculi it is composed of a series of superimposed laminæ, anastomosing together, and hence named by us the laminated sheath. The laminæ of the laminated sheath are formed of a trellis-work of fine connective-tissue fibres, covered with extremely delicate endothelial cells. The nerve fibres are not placed simply side by side within the laminated sheath, they are separated by delicate longitudinal fibres of connective tissue, between which are disposed large flat connective-tissue cells, which make impressions on one another. The different fasciculi composing a nerve are separated and united by ordinary connective tissue, composed of large fibres, between which connective-tissue cells, and sometimes adipose cells, are found. The blood-vessels of the nerve first ramify in the perifascicular connective tissue, then penetrating the interior of the fasciculi, they traverse the laminated sheath, and continue to ramify, finally forming a capillary network, with meshes elongated in the axis of the nerve. The lymph vessels do not penetrate the nervous fasciculi, but terminate in the perifascicular connective tissue. The plasma, however, which is exuded from the blood capillaries, after assisting in the nutrition of the nervous elements and becoming charged with their waste products, insinuates itself between the laminæ of the laminated sheath, and following a very complicated tract between them is finally lost in the perifascicular connective tissue, where it may be taken up again by the lymph vessels.

II. Pathological Histology of Nerves.

Congestion, hæmorrhage, and inflammation of nerves.—Congestion of nerves occurs rather frequently, as it is seen in all nerves implicated in an inflammatory focus; it may often extend beyond this focus: in phlegmon of the leg, for example, it is not rare to find congestion of the sciatic nerve extending as far as the sciatic notch. On carefully dissecting out the nerves involved in a wound they are found to be slightly swollen, and upon their surface are seen red lines parallel to their axes which indicate that congestion existed during life. Some observers, having examined nerves in wounds which were followed by tetanus, concluded that congestion of the nerves was the cause of the tetanus; thus Lepelletier, Curling, and Rokitansky refer traumatic tetanus to the extension of the congestion and inflammation to the nerves implicated in the wound. But this is surely an error, since such congestion may be observed in nerves in almost all slightly inflamed wounds, a condition which is however very rarely followed by tetanus. Congestion of nerves is much more frequent than is generally thought.

Hyperæmia particularly affects the perifascicular vessels, and may be easily recognised; hyperæmia of the intrafascicular vessels may also exist, but it is not so easily recognised by the naked eye, for the laminated sheath must be stripped off before the vessels filled with blood can be seen in the nervous fasciculi. To estimate the dilatation of capillaries, transverse sections of the nerve should be made, after hardening in chromic acid. Thus in a transverse section of the internal saphenous nerve, in a soldier who was suffering from a wound of the leg produced by the explosion of a shot, the intrafascicular capillaries were found dilated and filled with blood. In deep whitlow we have seen the collateral nerves present a similar lesion, and it is very probable that intrafascicular hyperæmia of nerves is an important cause of the acute pain accompanying this lesion. Congestion of nerves causes an increase of the blood tension and serous exudation into the perifascicular connective tissue; miliary hæmorrhages may also be produced. More extensive blood foci may be formed directly, when the nerves are denuded, as in wounds, for example.

Inflammation of nerves, characterised by congestion and serous exudation, is frequent as we have already seen, but suppurative inflammation is on the other hand rare in the nervous fasciculi. The laminated sheath opposes an almost insurmountable barrier to the diffusion of pus into the interior of the fasciculi : thus in a freely suppurating focus, nerves may be seen the peri-fascicular tissue of which may be the seat of hyperæmia, serous exudation, and even of diffuse suppuration, they having nevertheless preserved their functions. It is not without astonishment that on examining such nerves under the microscope, the nerve tubes are found to be completely normal. This resistance of the nerves may be attributed in a great part to the laminated sheath, but it is possible also that the numerous anastomoses of their blood-vessels, both in the perifascicular and intrafascicular connective tissue, put them, by securing independence of circulation, out of reach of morbid influences in their neighbourhood. This independence may be demonstrated by experiment, in fact it is possible to denude and separate the sciatic nerve throughout its whole extent in the thigh of a living animal, without the functions of the nerve being disturbed, or it becoming necrosed. The resistance of the laminated sheath to suppuration may also be proved by a similar experiment. If, after denuding the sciatic nerve, vermilion suspended in water be sprinkled on the wound, the lymph cells become charged with the coloured granules and carry them in various directions, but none of these coloured lymph cells are able to traverse the laminated sheath and fix themselves between the nerve tubes. It is not the same if this sheath has been torn; for example, if the nerve be traversed by a thread, the cells filled with the colour granules then find an open path and reach the interfascicular connective tissue.

Chronic inflammation or growing neoplasms have a much more important effect on nerves. The new cell formation, which characterises their evolution, being continued into the perifascicular connective tissue, and between the laminæ of the laminated sheath of the nervous fasciculi, separates them, compresses the fasciculi, and the nerve tubes undergo, below the diseased spot, the series of changes which are observed in the peripheral end of a divided nerve. The nerves of paralysed limbs in chronic hemiplegia accompanied with contracture of the extremities, are manifestly increased in size, so that they may be double their normal diameter. The nerve tubes have however preserved their normal structure, and the hypertrophy is solely due to thickening of the connective tissue.

In order to study the development of inflammatory and other neoplasms in nerves, it is not enough to dissect or dissociate them, but sections must be cut after hardening in a ·2 per cent. solution of chromic acid; in such sections it may be seen how first the perifascicular connective tissue, then the laminated sheath, and finally the intrafascicular connective tissue are successively invaded by cells of new formation.

Lesions following the section of nerves.—To study the various phenomena occurring after the section of nerves, recourse must be had to experiments on animals. The opportunities of studying these changes are rare in man, though in war wounds of the nerves are frequent, but the wounded either rapidly succumb or recover, exhibiting a series of symptoms similar to those seen in animals submitted to experiment.

Some observers, Förster among others, speak of the immediate union of nerves; it is very probable that they base their views on actual clinical facts, such as the rapid re-establishment of sensibility in a zone corresponding to the divided nerve. Arloing and Tripier have explained these facts by the existence of peripheral recurrent branches, and they based their interpretation on anatomical observations and physiological experiments. In animals, division of a nerve is never followed by immediate union, even when the two segments are kept together by a suture; hence, a similar union is doubtful in man. When a nerve is divided, the peripheral segment undergoes a peculiar degeneration, and after a variable time, never less than three months, it becomes regenerated. By this time union of the two segments of the nerve has taken place, though not by any of the processes admitted by surgeons; there is, in fact, neither immediate union, nor union by first intention, nor by second intention, nor by the aid of granulations: there is here a quite peculiar histological evolution.

Forty-eight hours after division of a nerve in a rabbit, and four days in a dog, the peripheral end of the nerve has lost its excito-motor power; but already before this period, important changes have taken place, in both the central and peripheral ends, and are continued till they finally end in the regeneration of the nerve, which first undergoes degeneration. In the first period, the peripheral segment of the divided nerve undergoes a series of changes, which have been considered as degenerative in nature; in the second, the nerve tubes which have been destroyed, at least in their essential parts, give place to new nerve tubes, which reconstitute the primary nerve.

Degeneration of divided nerves.—The changes which occur in the peripheral end of a divided nerve in the first few days following the operation were long looked upon as being entirely degenerative in nature; they seem to consist essentially in division of the myelin into fragments, drops, or granules, and finally its more or less complete disappearance by absorption. But in reality this decomposition of the medullary sheath of the nerve tubes is the consequence of an active development of the protoplasm of the interannular segment, so that if we preserve the name of degeneration for this process which ends in the destruction of the myelin, it must be remembered that it in no way signifies a passive process. Twenty-four hours after section of the nerve, when the functions of the peripheral segment are still preserved, the nucleus of each interannular segment of the nerve tube may be observed to be swollen, and the protoplasm surrounding it notably increased. The best method for observing these facts is to dissociate the nerve after allowing it to remain in a 1 per cent. solution of osmic acid. At the time that excitability is abolished, that is, forty-eight hours after division in a rabbit and four days in a dog, the nuclei and surrounding protoplasm of the interannular segments are so increased in size as to fill the whole calibre of the nerve tube; the medullary sheath and the axis cylinder are thus divided in two. The protoplasm is accumulated in the same way at different points in the length of the inter-annular segment, and, extending towards the axis of the tube, divides the medullary sheath and axis cylinder in two; thus the myelin is not only interrupted at the level of the interannular nucleus, but also at several other points in the length of the segment, sometimes even at its two extremities. It is thus seen that at the same time that the function of the nerve is abolished, the axis cylinder, which is essentially the physiological portion, is segmented, and is no longer able to transmit motor impulses. The relation is thus exact between the physiological phenomena and the histological changes observed. These lesions are completed in the following days, so that a week after division of the nerve the medullary sheath of the nerve tubes is decomposed into fragments, drops, or granules. Scattered in the protoplasm of the interannular segments are fine fatty granules, which stain a blackish yellow with osmic acid, while the myelin stains a bluish black with the same reagent. The nuclei of the interannular segments are multiplied, so that the activity of the interannular cells is shown, not only by increase of their protoplasm and hypertrophy of their nuclei, but also by their multiplication. At this time, therefore, the axis cylinders are decomposed into a series of fragments of unequal lengths, more or less folded and twisted, each being still surrounded by a layer of myelin.

At the same period, on the seventh day, granulo-fatty degenerative changes are observed in the cells of the interfascicular connective tissue, and in the endothelial cells of the blood-capillaries ramifying in it. These changes commence much earlier, but are now marked. The fat granules are probably derived from the myelin. The constituent fat of this substance is dissolved, passes in this state through the membrane of Schwann, to be finally fixed in the protoplasm of the connective-tissue cells and the endothelial cells of the capillaries. But these are not the only cellular elements located between the nerve tubes, which become loaded with fat granules; the lymph corpuscles also absorb fat and become changed into granular bodies.

The function of these lymph cells seems to be to transport into the general circulation part of the debris arising from the degeneration of the medullary sheath and axis cylinder. They are more numerous in the peripheral segment, near the point of section, than in the rest of the nerve, and at this spot they are loaded, not only with fat granules, but with actual droplets of myelin, which have escaped from the divided nerve tubes, and been taken up by the lymph cells. Some of the cells even penetrate the open tubes, travel into their interior, and become loaded with the granules of myelin they meet with in their passage. This migration of the lymph cells into the interior of the nerve tubes is particularly seen during the days following division of the nerve, and is seen not only in the peripheral but also in the central end.

The phenomena observed in the central segment must arrest our attention for a moment. Some observers (Neumann, Eichorst) have maintained that the changes in the nerve tubes in the central segment are the same as in the peripheral segment. These observers, unaware of the migration of the lymph cells into the medullated fibres, which we only recently discovered, have, doubtless, mistaken the modifications following this migration, for those constituting degeneration, properly so called, of the nerve tubes of the peripheral segment. In all points of the nerve tubes attacked by the lymph cells, the myelin is devoured by them; the axis cylinder itself cannot always resist them, and is itself sometimes partially destroyed. Changes in the nerve fibre result from this process, differing entirely from the lesions called degenerative; the myelin, instead of being simply broken into large fragments, which subsequently become smaller and smaller, is rapidly reduced into fine granules, which, acted upon by osmic acid, take a yellowish-brown stain. The migration of lymph cells into the central segment is generally arrested by the first annular constriction; sometimes, however, they pass it and may very rarely be found beyond the second node of Ranvier.

In from ten to eighteen days' time, when the wound of the cellular tissue and integuments has united by first intention, the extremities of the divided segments are swollen and are separated, though held together by a cicatricial tract. This cicatricial tract, which is much thinner than the nerve itself, is grey, and semi-transparent, and has the appearance of a non-medullated nerve filament, or a bundle of connective tissue ; there is then no union of the essential parts of the nerve, though the path of regeneration is traced.

Regeneration of divided nerves.—Regeneration of a nerve, or rather the preparatory phenomena, commence in the central segment, a short time after division ; but regeneration does not begin in the peripheral segment till many weeks later, and is continued for some months. Two or three days after division of a nerve in a rabbit, the axis cylinders of the nerve tubes of the central segment undergo hypertrophy near the point of section. They then seem to be very distinctly composed of fibrils —elementary nerve fibrils. Later, they divide longitudinally, bud and extend into the cicatricial cord. They are then non-medullated, and they divide and subdivide, so that a single nerve tube may give origin to a considerable number of new nerve fibrils. Still later, at a period which has not yet been accurately determined, for the process proceeds irregularly, the nerve fibres, hitherto without myelin, become covered with a medullary sheath, and assume all the characters of medullated nerve tubes; they have a membrane of Schwann and interannular segments, though these are relatively very short. It is only when the nerve tubes have attained all these characters that they can be easily recognised in preparations obtained by dissociation, after the action of osmic acid.

The new nerve tubes having thus reached the cicatricial cord, they may be seen to travel towards the peripheral segment and penetrate it. They are quite isolated in the midst of the old degenerated tubes, or, what is more frequent, they penetrate their interior. On dissociating the peripheral segment when regeneration has become tolerably advanced, that is from the seventieth to the hundredth day in the rabbit, old nerve tubes are found from which the myelin has entirely disappeared, except at certain spots where it still exists in the form of a granular mass. Within these tubes are found one, two, three, or even a much greater number of delicate medullated nerve fibres, with short interannular segments, and alongside them are found non-medullated fibres. Remak, who had already observed this important fact, explained it by an endogenous generation, resulting from the longitudinal segmentation of the old axis cylinder, which had been preserved. But we know now that in the peripheral segment of divided nerves the axis cylinders are first broken up and then entirely absorbed. The explanation of Remak cannot therefore be accepted, and in its stead we propose the following : the newly formed nerve tubes, developed within the old degenerated tubes, do not simply result from genesis *in situ*, but are produced from buds of the axis cylinders of the central segment, which, continuing to grow, first reach the cicatricial cord, then the degenerated segment, and extend either into the interior of the old nerve tubes, or between them. The membrane of Schwann, the cellular elements which line it, and the medullary sheath are alone formed from the proliferating cellular elements, which have accumulated in the interior of the old tubes.[1]

Waller has shown by numerous and ingenious experiments that the cause of degeneration of the peripheral segment of a divided nerve is separation from its trophic centre. The nutrition of nerves depends on certain nervous or ganglionic cells, which act as trophic centres to the nerves, so that they degenerate when separated from them. Thus the motor roots of the spinal cord have their trophic centres in the cord itself, while the sensory roots have their trophic centres in the spinal ganglia. Hence, on cutting both roots of a pair of nerves in the vertebral canal, the peripheral segment of the anterior root, and the spinal and central segment of the posterior root are only degenerated ; if a mixed nerve be divided at its issue from the vertebral canal, all that part of it which has been separated from its ganglionic centres undergoes degeneration.

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[1] For fuller details on this subject see *Leçons sur l'histologie du système nerveux*, by L. Ranvier 1878.

Tumours of nerves.—Besides **myelinic** and **amyelinic neuroma** (p. 237), **fibroma** (p. 166), and **myxoma** (p. 159), formerly called neuroma, are observed in nerves. **Carcinoma** and **epithelioma** generally affect nerves in consequence of extension of a tumour developed primarily in a neighbouring region. The perifascicular tissue is first invaded, the laminated sheath is dissociated by the new growth, and the nerve tubes undergo fatty degeneration and disappear. Förster has observed a case of primary carcinoma of the nerves which, increasing from the size of a lentil, finally developed and completely destroyed the nerve.

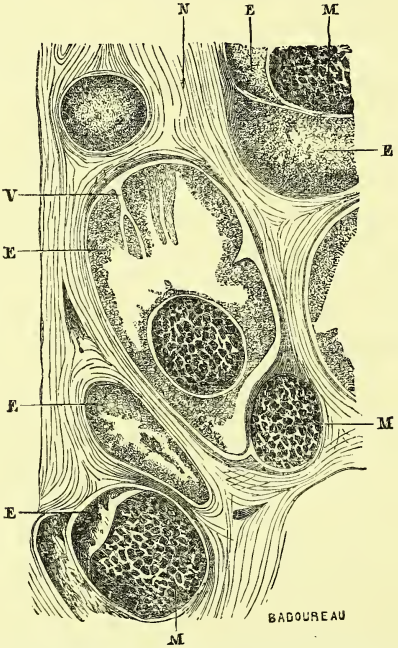

FIG. 257.—TRANSVERSE SECTION OF THE SCIATIC NERVE IN A CASE OF CYLINDRICAL-CELLED EPITHELIOMA, EXTENDING FROM THE UTERUS TO THE NERVE.

The interfascicular connective tissue N is invaded by epithelial lobules of new formation E, which are also developed in the laminated sheath. The nervous fasciculi, M, are on the contrary respected. Magnified 40 diameters.

CHAPTER XV.

LESIONS OF THE CEREBRUM AND CEREBELLUM.

I. Normal Histology of the Central Nervous System.

THE central nervous system consists of the cerebrum, cerebellum, Pons varolii, medulla oblongata, and spinal cord. The spinal cord will be considered in the next chapter.

Cerebrum.—The cerebrum, like all other parts of the central nervous system, is composed of two symmetrical halves or hemispheres, and is produced by the expansion of all the nervous fasciculi, which pass from the spinal cord through the medulla oblongata, Pons varolii, and crura cerebri. The nervous filaments which convey sensory impressions, or conduct voluntary motor impulses to the periphery, terminate in the cerebral grey centres, which are essentially composed of nerve cells. These centres are found in the grey matter of the cortex of the convolutions, and in the central grey nuclei, or ganglia of the brain—the optic thalami, corpora striata, corpora quadragemina, and the ganglionic origins of the cranial nerves. The cerebrum is, in a general way, composed of a covering of grey matter, in which terminate the white fasciculi, which have entered through the pyramids, and spread out into the white substance of the centrum ovale and corona radiata. In the midst of this white substance the ventricles are excavated, in the walls of which appear the grey matter of the optic thalami and corpora striata.

We do not propose to give here an exhaustive description of the structure of the brain, nor to describe in detail the course, still so ill understood, of the nervous fasciculi which pass from the crura to the cortex of the convolutions, nor the course of the radicular fasciculi of the cranial nerves to their deep origins; we shall content ourselves by recalling the external topography of the convolutions and their structure. The topographical anatomy of the convolutions, regarded as the expansion of certain fasciculi of the peduncles, should indeed always be present to the memory when making an autopsy, so as to be able to exactly determine the seat of any lesion. Studies on the localisation of cerebral diseases have been prosecuted by Broca, Fritch and Hitzig, Ferrier, Charcot, Duret, Lépine, Pitres, Grasset, etc., with such important results that we are obliged to consider them, even in a treatise of pathological histology; otherwise we should be unable to indicate the lesions which correspond to perfectly well-defined pathological types, such as aphasia, hemi-anæsthesia, hemi-chorea, etc.

Topography of the cerebral convolutions.—The surface of the hemispheres is divided into four lobes, the frontal, parietal, temporal, and occipital lobes. To fix the limits of these convolutions

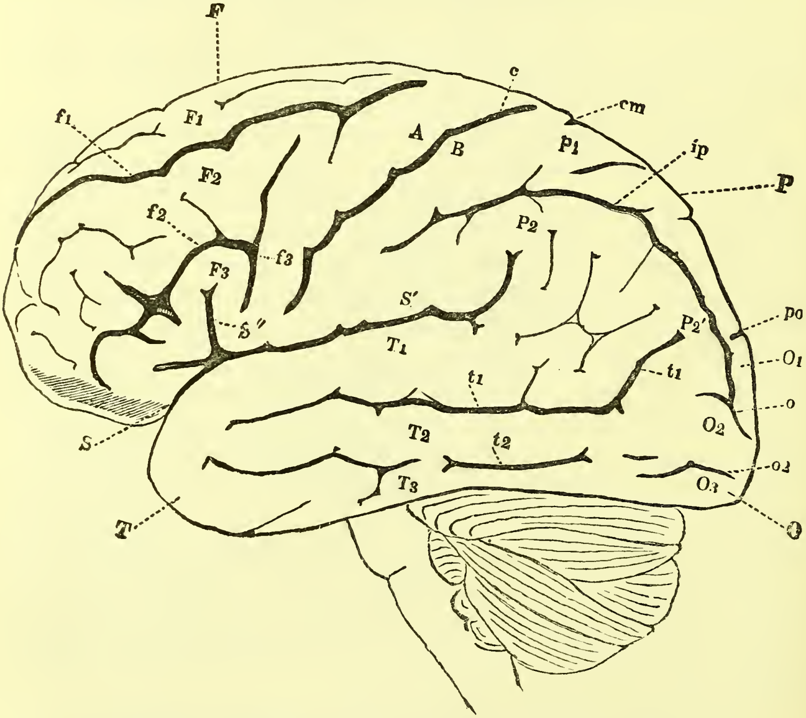

FIG. 258 (from Ecker).—LATERAL VIEW OF THE HUMAN BRAIN.

F, frontal lobe ; P, parietal lobe ; O, occipital lobe ; T, temporo-sphenoidal lobe ; S, fissure of Sylvius ; S′, horizontal, S″, ascending sulci of the same ; C, sulcus centralis, or fissure of Rolando ; A, ascending frontal convolution ; B, ascending parietal convolution ; F_1, superior, F_2, middle, F_3, inferior frontal convolution ; f_1, superior, f_2, inferior frontal sulcus ; f_3, sulcus præcentralis ; P_1, superior or posterior parietal lobule ; P_2, inferior parietal lobule, or gyrus supramarginalis ; P_2', gyrus angularis ; *ip*, intraparietal sulcus ; *cm*, termination of the calloso-marginal fissure ; O_1, first, O_2, second, O_3, third occipital convolution ; *po*, parieto-occipital fissure ; o_1, transverse occipital sulcus ; o_2, inferior longitudinal occipital sulcus ; T_1, first, T_2, second, T_3, third temporo-sphenoidal convolutions ; t_1, first, t_2, second temporo-sphenoidal fissure.

the fissure of Sylvius and the fissure of Rolando must first be determined. First, in front of the fissure of Rolando is the **frontal lobe**, consisting of four principal convolutions, the ascending frontal (A, fig. 258), along the anterior margin of the fissure of Rolando, and three convolutions running horizontally from behind forwards, and called respectively the first, second, and third frontal convolutions. Second, the **parietal lobe** is limited in front by the fissure of Rolando which separates it from the frontal lobe, and below by the fissure of Sylvius (s' and s'') which separates it from the temporal lobe, its posterior border being formed by the parieto-occipital fissure, *po*, which is not, however, well marked in man. The parietal lobe consists of two principal lobules or convolutions, the ascending parietal convolution, B, bordering the fissure of Rolando and continuous with the superior parietal lobule P_1, and the inferior parietal lobule P_2 and gyrus angularis. At the upper part, the ascending frontal convolution A, and the ascending parietal convolution B, are continuous on the internal surface of the hemisphere with the paracentral lobule. Third, the **temporal lobe** is formed of three parallel and similar convolutions, which have been called the first, second, and third temporal convolutions, T_1, T_2, and T_3, fig. 258. Fourth, on the internal surface of the hemisphere, above the corpus callosum, is found the gyrus fornicatus or marginal convolution of the corpus callosum, then the calloso-marginal fissure, above which is met with, from before backwards, the internal surface of the third frontal convolution, the paracentral lobule, the quadrate lobule or Præcuneus, the parieto-occipital fissure (*po*, fig. 258), the cuneate lobule, and the occipital lobe with its three convolutions (O_1, O_2, O_3, fig. 258).

Structure of the convolutions.—The grey cortex of the cerebral convolutions contains, in the frontal and parietal lobes, cells, varying in size and shape, round, pyriform, and fusiform, as well as nerve fibres and a granular ground substance. These elements are arranged in such a way that three more or less definite layers may be distinguished. They have been described by Meynert. The most superficial, just beneath the pia-mater, contains delicate medullated nerve tubes parallel to the surface of the brain, and a few small nerve cells disseminated in a granular ground substance. The second layer contains a large number of small pyramidal nerve cells pointing towards the surface of the convolution; these cells give this layer a grey colour (2, fig. 259). The third layer is characterised by pyramidal cells, some of medium size, others so large that they deserve the name of giant cells; they may even attain the diameter of 40 μ or 50 μ, and equal in size the large cells of the anterior horns of the spinal cord. Their bases are turned towards the deep layers of the convolutions, and their elongated bodies terminate in a point directed towards the surface of the brain; they give off more or less numerous and ramifying branches, which spring either from their body or from their attenuated extremity; at their base they receive a single nerve tube, which loses its myelin before entering the cell, and which corresponds to Deiters' process. Between these large cells, which are especially found at the bottom of the third layer, pass fasciculi of medullated nerve tubes in a direction perpendicular to the surface of the convolution. The fourth layer contains a few small globular cells, and the fifth fusiform nerve cells. These two layers are traversed by the fasciculi of nerve tubes, which terminate in the pyramidal cells. The large pyramidal cells are not found in all parts of the cortex; they are, according to Betz, localised in portions of the frontal and parietal lobes, which are, according to Fritch and Hitzig, the psycho-motor centres, and also in the marginal convolutions of the fissure of Rolando and the paracentral lobule. The convolutions of the occipital and sphenoidal lobes are constituted on the same model, with the exception that pyramidal cells are rarer, and giant cells are altogether wanting.

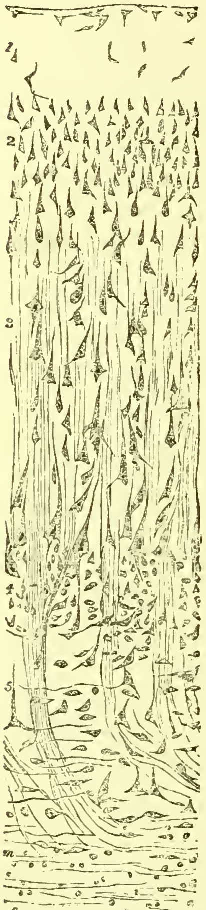

Fig. 259.—Section of the Grey Cortex of the Third Frontal Convolution (after Meynert).

1, superficial layer of scattered corpuscles; 2, dense layer of small pyramidal corpuscles; 3, layer of large pyramidal corpuscles; 4, dense layer of small irregular corpuscles; 5, layer of fusiform corpuscles; *m*, medullary fasciculi. Magnified 75 diameters.

Localisation of function.—According to data furnished by physiological experiments, and by observations in human pathology, the grey motor centres of the limbs are localised in the convolutions bordering the fissure of Sylvius and the paracentral lobule. These centres are represented in the adjoining diagram (fig. 260), which we have borrowed from the memoir of Charcot and Pitres, on motor localisation in the grey matter of the brain.[1] The middle third of the ascending frontal convolution is the centre of isolated movements of the inferior extremity (3, fig. 260). The paracentral lobule, the superior third of the ascending frontal convolution, and the two superior thirds of the ascending parietal convolution, are the centres for movement of the superior extremity on the opposite side of the body (4, fig. 260). The

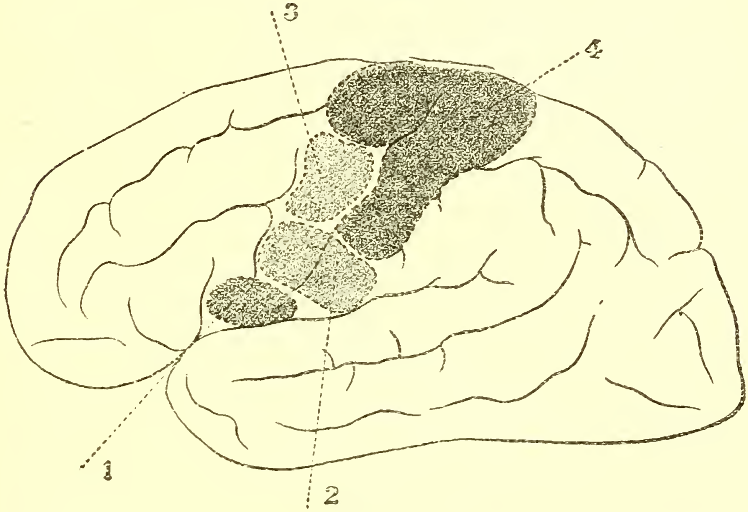

FIG. 260.

motor centre of the lower part of the face is localised in the lower extremity of the ascending frontal and ascending parietal convolutions (2, fig. 260). The posterior part of the third left frontal, or Broca's convolution, is the seat of articulate language; it should be added, however, that the convolutions of the island of Reil, touching the base of the third frontal convolution, also participate in presiding over the function of speech.

According to Charcot and Pitres, from whom we have borrowed this *résumé*, it must not be concluded that these centres, attributed from experimental data to motor functions, have exact geometrical limits; they vary in a certain measure among different animals, but it is none the less true that, in the superior mammifers, monkeys for example, motor zones are distributed in the cerebral grey matter according to a general plan, which is found again in man.

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[1] See *The Localisation of Cerebral Diseases*, by David Ferrier, M.D. Smith, Elder, & Co.

It is generally admitted that the anterior part of the frontal lobe is the seat of intelligence, and it is believed that the posterior region of the cerebral cortex, the posterior part of the parietal and temporal lobes and the occipital lobe, receive sensory impressions.

The internal capsule.—Most authors admit that the motor fibres which constitute the inferior plane of the crus cerebri, are connected with the cells of the corpus striatum, before passing to the convolutions, and that the sensory nervous fasciculi, which pass through the superior half of the crus, are in relation with the optic thalamus. Much, however, remains to be discovered before an exact knowledge of the structure and functions of these organs is obtained. It is, however, at the present time pretty completely established that destructive lesions, produced by softening or hæmorrhage of the internal capsule, cause, according to the spot affected, either motor hemiplegia, with permanent contracture of the extremities, or hemi-anæsthesia, general or special. The internal capsule (11, fig. 261) situated between the optic thalamus

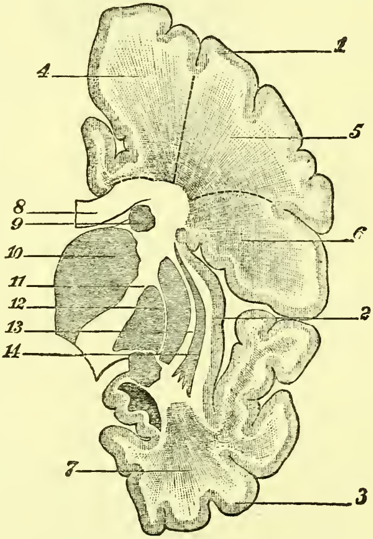

Fig. 261.—Section of the Frontal Lobe (after Pitres).

1, ascending frontal convolution; 2, island of Reil; 3, sphenoidal lobule; 4, 5, 6, superior, middle, and inferior frontal convolutions; 7, sphenoidal convolution; 8, corpus callosum; 9, nucleus caudatus or interventricular portion of the corpus striatum; 10, optic thalamus; 11, internal capsule; 12, nucleus lenticularis or extraventricular portion of the corpus striatum; 13, external capsule; 14, the claustrum.

and the corpus striatum is an emanation from the inferior stage of the crus cerebri; it contains fibres passing directly from the crus to the grey cerebral cortex, and particularly a fasciculus which, according to Meynert, is exclusively sensory, and which encircles the lenticular nucleus to pass to the surface of the occipital lobe. The indirect fibres, which pass from the crus to the nucleus lenticularis, and to the optic thalamus, or which pass from these centres, reach

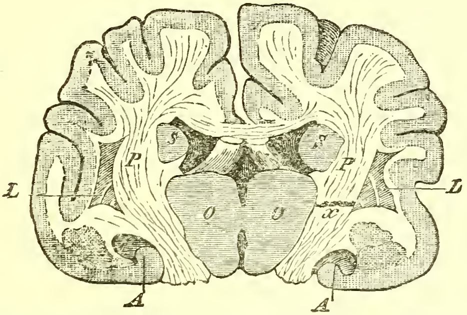

Fig. 262.—Transverse Section of the Brain of a Dog at the Level of the Corpora Albicantia (Carville and Duret).

O, O, optic thalami; S, S, nucleus caudatus of the corpus striatum; L, L, nucleus lenticularis of the corpus striatum; P, P, internal capsule or peduncular expansion; A, A, hippocampus; *x*, section of the posterior part of the internal capsule producing hemianæsthesia.

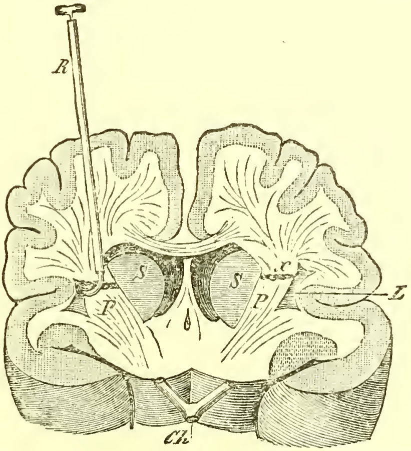

Fig. 263.—Vertical Transverse Section of the Brain of a Dog, Five Millimetres in front of the Optic Commissure (Carville and Duret).

S, S, nucleus caudatus of the corpus striatum; L, L, nucleus lenticularis of the corpus striatum; P, peduncular expansion; *ch*, chiasma of the optic nerves; *x*, section of the peduncular expansion producing motor hemiplegia; *r*, a stylet by which the internal capsule is divided.

the cerebral cortex by traversing the internal capsule; hence, it gives passage to almost the whole of the fibres which unite the cortex and the central nuclei to the periphery. Observations, which are now very numerous, the first of which were published by Türck in 1859, have established the fact that lesions of the most posterior part of the internal capsule, cause hemiplegia with hemi-anæsthesia of cerebral origin, and troubles of all the special senses. If, on the contrary, the lesion falls on the middle or anterior part of the internal capsule, there is complete hemiplegia without hemi-anæsthesia, but with permanent contracture of the extremities; descending degeneration of the pyramidal fasciculi is then observed in the Pons Varolii and medulla oblongata (see later, Secondary Degenerations of the Spinal Cord, p. 612). Experiments on dogs have confirmed these facts. Carville, Duret, and Veyssière have succeeded in reaching and lacerating the internal capsule. If the posterior segment is torn, as at *x*, fig. 262, hemi-anæsthesia is produced; if the anterior segment, as at *x*, fig. 263, is divided, motor hemiplegia results.

The cerebellum.—The cerebellum is formed on the same general plan as the cerebrum, namely, of white fasciculi passing

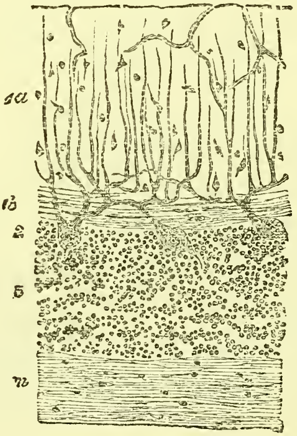

Fig. 264.—Section of the Cerebral Cortex (after Meynert).

1 *a*, external layer of grey matter; 1 *b*, internal part of the same layer containing fusiform cells and arched fibres; 2, layer of the cells of Purkinje; 3, granular layer; *m*, white substance of the medullary nerve tissue.

from its crura, which bring it into communication with the medulla oblongata and with the grey centres of the cerebrum, so that each cerebellar hemisphere is connected with the cerebral hemisphere of the opposite side. A nucleus of grey subtance, the corpus dentatum is situated at the centre of the white substance, the cortex being also formed of grey matter, which however differs greatly in structure from that of the cerebrum. According to Meynert, on proceeding from the surface to the deep parts there may be seen successively: first, a rather thick granular layer containing a few ganglionic cells (1 *a*, fig. 264); secondly, a thin layer traversed by medullated nerve tubes and fusiform cells; thirdly (1 *b*, fig. 264), a layer of large nerve cells, the cells of Purkinje, which send their ramifying protoplasmic processes into the two preceding layers, they have also a single axis cylinder process, called the process of Deiters, which penetrates the deep layers; fourthly, a granular layer of small round cells, and finally the white substance composed of nerve fibres.

Cerebral circulation.—The internal carotid and the vertebral arteries, united in the basilar trunk, contribute to form the circle of Willis at the base of the brain. The three principal arteries given off from the circle of Willis are the anterior cerebral, the middle cerebral or Sylvian artery, both springing from the internal carotid, and the posterior cerebral, a branch of the basilar. We do not propose to trace all their branches, notwithstanding the interest attached to some of them, for example the various ramifications of the Sylvian artery; but, referring our readers to the works of Duret, we would here simply draw attention to certain peculiarities of their distribution, which are important in the pathogenesis of the brain. The branches of the three cerebral arteries, distributed to the convolutions, penetrate the grey matter after crossing the pia mater. The first layer of the cortex is less vascular than the succeeding layers; that which contains the pyramidal cells possesses a rather close capillary network. The same arteries, after furnishing this capillary network, continue their course perpendicularly to the surface of the brain, and, penetrating the white substance, they anastomose by their extremities with the arterioles of the white substance. These anastomoses take place by means of extremely fine twigs, an arrangement which favours the production of infarctus by embolism. Cortical infarctuses (softened yellow patches of the convolutions) implicate thus, to a certain depth, simultaneously the cortex and the white substance of the convolutions. The arterioles, given off at the origin of the cerebral arteries, penetrate at once to the base of the brain to reach the grey nuclei and central parts; thus the Sylvian artery furnishes

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arterioles, which perforate the locus perforatus to be distributed in the corpus striatum. Most of these arterioles belong to what Cohnheim has called the system of terminal arteries, that is, those which do not anastomose together, but which terminate in an isolated manner, an arrangement most favourable for the production of infarctus, and softening by vascular obstruction. In the territories of those arteries which are distributed to the grey centres of the brain, hæmorrhages are also frequently found. White ischæmic softening is frequent in the cerebral cortex, hæmorrhage is rare. This lesion is, however, very frequent in the corpora striata, optic thalami, etc. The causes of hæmorrhage in the central organs are, according to Duret: first, the mode of origin of the arteries, which spring almost directly from the circle of Willis; secondly, the size of the arterioles, which is relatively considerable—these two conditions cause the cardiac impulse to be directly transmitted with great force; thirdly, the absence of anastomoses, which renders rupture easy, there being no possibility of collateral circulation of the blood when some obstacle is presented to its course.

II. Lesions of the Meninges.

The lesions of the cerebral and spinal meninges being similar, a general description is only given here, anything peculiar to the spinal meninges being separately considered.

Congestion and inflammation of the meninges.—Congestion, varying in intensity, is very frequent in the pia mater where it may be active or passive. Active congestion, when severe, causes desquamation of the epithelium lining the great arachnoid cavity, exudation of an albuminous fluid and extravasation of a varying number of white blood corpuscles.

In **cerebral rheumatism** the pia mater is congested throughout its whole extent, and shows patches where the congestion is more intense, and effusion of blood may take place. These patches are of a bright red colour, as if the blood in the vessels was highly oxygenated; shreds of the arachnoid and pia mater, thus altered, show, when examined without the addition of water, regular or fusiform dilatation of the blood-vessels, around which the red corpuscles are often extravasated. The choroid plexuses are congested, as well as the velum interpositum. The fluid contained in the arachnoid cavity in the ventricles and the subarachnoid spaces is increased in quantity, and in it are found a number of large granular epithelial cells and white blood corpuscles, though it is not very turbid. When cerebral rheumatism has lasted twenty-four hours or more, the fluid contained in the arachnoid, ventricles, and sub-arachnoid spaces is more abundant and cloudy, and even slightly puriform, which appearance is due to the larger number of epithelial cells and white blood corpuscles it then contains. This condition is not peculiar to cerebral rheumatism, it may be found in all forms of cerebral congestion accompanied with delirium, such as may be caused by pneumonia, variola, typhoid fever, etc.

Primary cerebral meningitis is extremely rare; it may be caused by sunstroke. When the inflammation extends over the whole surface of the nervous centre, as in cerebro-spinal meningitis, it is generally epidemic, such as breaks out in armies and hospitals. The most frequent form of meningitis is that which follows tuberculosis, or tumours of the meninges or brain. **Acute meningitis** is characterised by the presence of pus on the surface of the pia mater, by thickening and cloudiness of the connective tissue of this membrane, and by the accumulation of pus cells around and along the vessels where the connective tissue is most abundant. The blood-vessels appear to the naked eye to be surrounded by an opaque zone, and on examining them under the microscope the loose connective tissue around them is seen to be filled with lymph cells, which accumulate also in the perivascular sheaths, and envelope them like a sleeve. The sero-purulent fluid found on the surface of the membrane, and accumulated in the anterior and posterior sub-arachnoid spaces, is sometimes very thin, at others thick and mixed with fibrin, as in peritonitis.

When the meningitis is acute and has lasted many days, the pus, mixed with fibrin, forms under the visceral arachnoid a continuous, opaque, yellowish layer, which is thicker over the sulci, and separates the convolutions. The blood-vessels are partly imbedded in this false membrane, and appear like red lines covered with a veil. This fibrinous layer may be 5 mm. in thickness above the sulci. On raising the meninges, infiltrated with pus, the cerebral grey matter is seen beneath covered with red spots. On section it is seen that each red spot corresponds to a blood-vessel, which, examined under the microscope, is seen to be surrounded by a layer of pus mixed with a varying number of blood corpuscles.

In **cerebro-spinal meningitis** a similar exudation is found round the spinal cord and pons varolii. The pus fills the sub-arachnoid cavity of the spinal cord, and the meshes of the spinal pia mater, but it does not penetrate beneath the fibrous part of this membrane. The grey matter of the spinal cord is of a pinkish colour. In sections, made according to the classic method, no modification of the nerve elements can be found, but simply hyperæmia of the blood-vessels of the pia mater, and pus cells between its connective-tissue fasciculi. Sometimes suppuration is so rapid that the quantity of pus is considerable, even when the symptoms of the disease have hardly lasted a few hours.

Tubercular meningitis.—The lesions of tubercular meningitis do not differ from those of simple meningitis just described, except by the presence of tubercles which are found chiefly along the blood-vessels of the pia mater; the exudation is the same in the two diseases. Tubercular meningitis is, however, frequently mistaken for acute primary meningitis, for the tubercles are apt to be overlooked, but the presence of small and numerous granulations will be discovered on attentive examination. To find them the pia mater should be removed from those regions where tubercle is most frequently found, such as the fissure of Sylvius, and the superior crura cerebelli. The piece of membrane should then be agitated in water till the adhering fragments of cerebral tissue are separated, and on holding it up to the light small whitish spots will be seen in the membrane. This examination

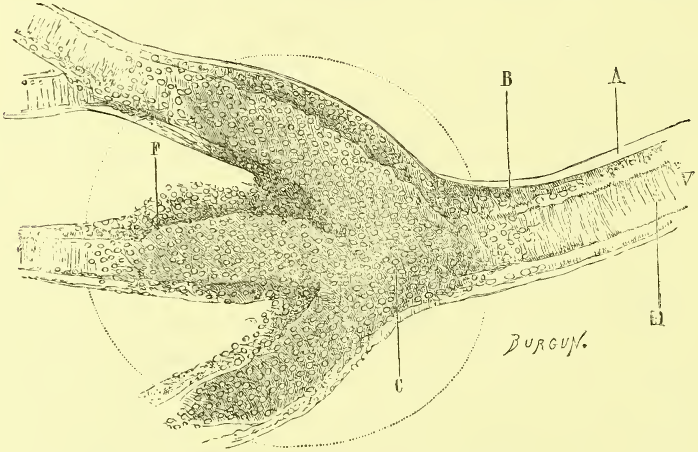

Fig. 265.—Blood-vessel of the Pia Mater, passing through a Tubercular Granulation, the limits of which are indicated by the dotted line.

A, perivascular sheath ; B, vascular wall ; F, elements contained in the sheath ; C, coagulated fibrin in the blood-vessel. Magnified 100 diameters.

must not, however, be considered sufficient. The pia mater should be carefully spread upon a glass slide, when with a low power granulations will be perceived which were not before recognisable with the naked eye, and which are seen to be particularly numerous in that part of the pia mater which dips down between the convolutions springing from the fissure of Sylvius.

In studying one of these granulations minutely, it is seen to be formed of lymph or embryonic cells accumulated round a blood-vessel. The large granulations encroach upon the neighbouring tissue and completely surround the perivascular sheath. The blood-vessel which is in the centre of the granulation is generally obliterated by a fibrinous coagulum. These masses of cells are most frequently found at the point of bifurcation of a small blood-vessel, where the perivascular sheath is wider; it is also not unusual to see many granulations arranged like a rosary, at short distances from each other along the same blood-vessel. The new tissue often ensheathes the blood-vessel for a certain distance; it is composed of small elements, pressed closely together, and situated both in the perivascular sheath and pia mater.

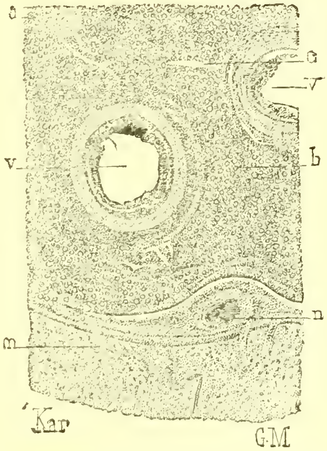

FIG. 266.—SECTION OF TUBERCULAR MENINGES.

a, small obliterated vessel; v, v, much larger vessels. The internal coat of these vessels is greatly thickened, and in the internal layer of the vessel, which is in the centre of the figure, are seen two giant cells; *n*, vessel obliterated near the cerebral substance, *m*. Magnified 40 diameters.

In order to make a thorough examination of meninges infiltrated with tubercle, the membranes and subjacent cerebral tissue should be well hardened, first in Müller's fluid and then in gum and alcohol. Sections cut perpendicularly to the surface show more or less altered blood-vessels contained in the tubercular tissue. In the deep layers of the thickened pia mater the capillaries, surrounded with a mass of newly formed cells, are seen to pass vertically into the cerebral substance (in fig. 266). These small vessels are often included in a true tubercular granulation, at the spot where they pierce the grey matter which is itself inflamed.

The small arteries and veins of a tubercular pia mater show a very remarkable thickening of their intima. In a case published[1] by one of us, the thickened internal coat of the arteries showed quite a peculiar structure. It was bordered internally by the usual endothelial layer; but it contained, besides, large cells, flattened by reciprocal pressure, drawn out to a point and implanted perpendicularly on the surface of the middle coat (*vide* fig. 267), forming a series of superimposed layers. In the midst of these, still larger cells were found containing two or three nuclei, and true giant cells containing fifteen to twenty nuclei. In fig. 267 the isolated elements are shown, and in fig. 268 the giant cells, seen in a section of tubercular endarteritis, under a high power. The internal coat, affected with tubercular inflammation characterised by the formation of giant cells, was almost uniformly thickened without definite tubercular nodules being produced. Thus, in the midst of discrete or confluent tubercles,

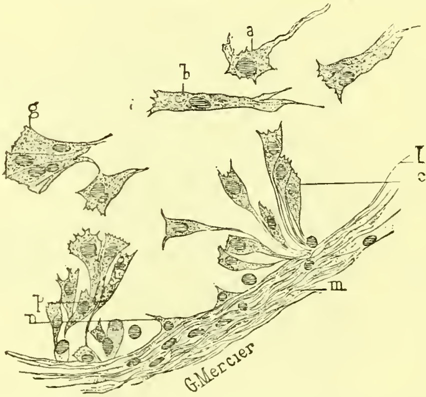

FIG. 267.—TRANSVERSE SECTION OF THE INTERNAL COAT OF AN ARTERY, AFFECTED WITH TUBERCULAR ENDARTERITIS, AT ITS JUNCTION WITH THE MIDDLE COAT.

m, middle coat; *n*, triangular cells with their bases attached to this coat; *c*, *p*, very long prismatic cells inserted on to the middle coat by their pointed extremities; *a*, *b*, isolated cells of the internal coat; *g*, multinucleated cells. Magnified 300 diameters.

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[1] *Journal de l'Anatomie*, t. xvi. p. 213; 1880.

blood-vessels may be found affected with a peculiar form of endarteritis, in which the coats and perivascular sheaths are infiltrated with small cells, and are lodged in a connective tissue filled with the same elements.

The giant cells, which are so common in tubercle of all the other organs, are very rare in tuberculosis of the meninges: we ourselves have only observed them in the solitary case reported above, and in which their presence was limited to the inflamed internal coat. The absence of giant cells in tubercular meningitis may be explained by the rapidity with which the meningitis is developed, which is too great to allow them time to form. This is only a hypothesis which seems plausible till fuller information be forthcoming.

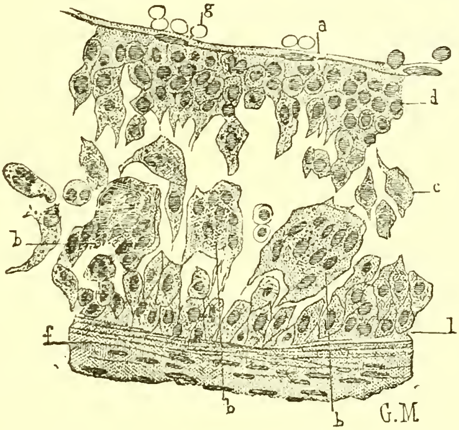

FIG. 268.—SECTION OF INFLAMED AND TUBERCULAR INTERNAL COAT.

a, layer of flat endothelial cells indicating the internal border of the inflamed inner coat; *g*, red blood corpuscles circulating in the lumen of the vessel; *d*, layer of round or polygonal cells; *b*, *b*, *b*, giant cells; *l*, layer of cylindrical and round cells at the base of the inflamed inner coat; *f*, middle coat. Magnified 200 diameters.

In certain cases of tubercular meningitis, the pia mater and arachnoid of the spinal cord are scattered over with granulations.

Chronic meningitis.—The most common form of chronic meningitis is *diffuse meningo-encephalitis*, a disease characterised by that group of symptoms called *general paralysis of the insane.* The principal morbid phenomenon is thickening of the pia mater, caused by a new formation of connective tissue; the walls of the blood-vessels undergo a similar thickening; those which pierce the cerebral tissue are adherent to it, so that this substance is torn on removing the pia mater; there is also proliferation of the connective tissue of the cerebrum, diffuse interstitial encephalitis, and atrophy with pigmentation of the cells of the cortical layer of the convolutions (*vide* p. 596). In some cases there is also a peculiar degeneration of the walls of the blood-vessels, which lesion, described by Magnan as that of colloid degeneration, seems to us to consist in chronic endarteritis and periarteritis.

Pachymeningitis.—Inflammation of the dura mater has received the name of pachymeningitis; it may be external or internal, and is generally chronic.

In **internal pachymeningitis** small granulations or buds are formed on the internal surface of the inflamed dura mater; they contain vascular loops continuous with the pre-existing blood-vessels of the membrane; these granulations spread over the surface of the dura mater, and constitute a thin and very vascular false membrane of newly formed connective tissue. When recent the blood-vessels it contains have embryonic walls; they are fragile and often rupture, and blood is effused into the arachnoid sac or into the tissue of the false membrane, which is then ecchymosed. These ecchymoses may be easily mistaken for simple spots of blood on the surface, if, after spreading the membrane carefully on a slide, a close network of blood-vessels are not distinguished and new connective tissue, the meshes of which contain extravasated red blood corpuscles. When the false membrane is older, large masses of reddish-brown blood pigment are found round the blood-vessels, and even crystals of hæmatoidin. The membrane is often composed of several superimposed parallel layers. When in consequence of vascular ruptures a quantity of blood is effused between the layers of these multiple false membranes, blood cysts are produced, known by the name of *hæmatomata of the dura mater*. For a long time it was thought that, in these cases, the blood was effused upon the surface of the dura mater, and surrounded with a layer of fibrin, which became organised into a false membrane, encysting the hæmatoma.

External chronic pachymeningitis, or inflammation of the external surface of the dura mater, differs from the preceding. By adhering to the bones of the skull, the dura mater plays the rôle of a periosteum, and its lesions are most frequently related to those of the internal plate of the bones of the skull; thus, external pachymeningitis is generally caused by disease of the bones, due to syphilis or wounds; in alcoholism, thickening of the whole dura mater may often be observed, accompanied with hæmorrhagic internal pachymeningitis.

Syphilis, in its tertiary period, often simultaneously affects the dura mater and the bones of the skull. Inflammatory and gummatous new growths are then developed in the layer of the dura mater in contact with the bone, so that inflammatory granulations, or gummata, are developed simultaneously on the external surface of the dura mater, in the medullary canals of the internal plate, and in the diploe. The pathological phenomena then observed between the dura mater and the bone are similar to those observed between the latter and the epicranial periosteum.

External syphilitic pachymeningitis is characterised by numerous conical buds and excrescences, in the form of pointed papillæ, or which ramify like a cauliflower; they are grey or pink and semi-transparent, and composed of a rather friable tissue, which is exposed when the calvarium is removed. These excrescences extend over a great part of the dura mater; they are lodged in hiatuses of the bone substance, and are directly continuous with the medullary tissue. In structure they resemble the granulations of inflammation. The medullary tissue inflames, the bony lamellæ of the diploe undergo absorption, and show the same histological appearances as were described in rarefying ostitis (*vide* p. 332). When in contact with the osseous lamellæ, the granulations, which spring from the dura mater and the inflamed medullary tissue, contain a great number of giant cells, lodged in the notches left by the absorbed osseous tissue. In cases where external syphilitic pachymeningitis is very intense, the ostitis extends to the external surface of the bone, and granulations are developed on the epicranial periosteum, similar to those of the dura mater: the entire bone then becomes riddled with holes like a colander.

Tumours of the meninges. Fibroma.—The Pacchionian bodies may be described with fibroma, for when developed in great numbers they form true tumours, capable even of causing perforation of the bones of the skull; they also contain numerous and dilated blood-vessels. They are composed of layers of fibrous tissue and flattened cells, resembling in structure the fibrous plates of the spleen—lamellar fibroma (*vide* p. 163). They exist in the normal condition, and only acquire pathological importance by their exaggerated development, which often seems to be due to alcoholism. Their structure is quite characteristic, and has nothing in common with that of tubercular granulations, for which these bodies have been mistaken; they are often incrusted with calcareous salts. True fibromata, adherent to the dura mater, have been seen, but they are very rare.

Cysts.—Small serous cysts, developed from vascular buds, are often found in the choroid plexuses; similar cysts are also found in the sub-arachnoid cellular tissue, particularly near the fourth ventricle.

Syphilitic gummata.—The cerebral meninges are rather frequently the seat of gummata. They form small spherical tumours, generally about the size of a small pea, on the external surface of the dura mater. They are located in cavities, hollowed in the bones of the skull; their centre is caseous when they are old; they may be followed by all the accidents of ostitis and necrosis, with the formation of purulent foci, as already described on page 340. Gummata of the pia mater and arachnoid, which are much rarer than those of the dura mater, may attain a much larger size. They develop towards the brain, which they invade for a more or less considerable extent, producing a surrounding zone of encephalitis.

Tubercle.—Tubercles are generally found only in the pia mater and sub-arachnoid cellular tissue: they may, however, be met with in the false membranes of the dura mater.

Sarcoma is very frequent in the dura mater, in which the lesions of pachymeningitis are consecutively produced. Two forms of sarcoma may be seen, as in the brain—neurogliac sarcoma, often developed in the course of the cranial nerves, and angiolithic sarcoma, frequently observed on the internal surface of the dura mater, in the sub-arachnoid cellular tissue, and in the choroid plexuses (*vide* p. 144).

Carcinoma and **Epithelioma** are very rare in the meninges, where they are always secondary.

All tumours of the dura mater may perforate the bones of the skull. Such perforations are therefore not peculiar to syphilitic gummata, for secondary sarcomata and carcinomata may cause similar lesions. Thus inspection of a dried cranium, showing losses of substances similar to those produced by gummata, cannot decide what was the nature of the neoplasm causing the lesion.

III. Lesions of the Cerebrum and Cerebellum.

Cerebral anæmia is solely characterised by pallor of the nervous substance, unaccompanied with any appreciable change in the cells.

Cerebral congestion.—When cerebral congestion has lasted some time, it always leaves traces after death; injection of the blood-vessels is marked, the convolutions are pink, increased in size, and sometimes so closely pressed together that the sulci are almost effaced. Upon the surface of the brain reddish patches or spots are sometimes met with. On making a section of the brain at one of these patches, the cortex is seen to be of a pinkish grey colour, and the white substance to be spotted over with red points, caused by the division of capillaries filled with blood. These red points, when numerous and near together, give the brain tissue a speckled appearance. On examining microscopic sections cut at the level of the red patches, red blood corpuscles, and even yellow and red pigment granules may be recognised in the perivascular sheaths; they are accumulated at the spots where the blood-vessels bifurcate, and the sheath is separated from the vascular wall by a wide space. The nerve cells and elements of the neuroglia do not seem to be altered, neither in the red patches nor around them. It may be noted in passing that repeated attacks of congestion, accompanied with diffuse meningo-encephalitis, cause pigmentation of the nerve cells.

Œdema of the cerebrum.—Accumulation of fluid in the ventricles and sub-arachnoid spaces, accompanied with anæmia and softening of the fornix, is called œdema of the cerebrum. No histological lesion corresponds to this condition, which is simply due to imbibition of serum by the cerebral substance. The principal cause of œdema is pressure upon the veins of Galen, and the development of tubercular granulations around them. Softening of the fornix, which coincides with an accumulation of serum in the ventricles, occurs as a rule in tubercular meningitis.

Lesions of the cerebrum in melanæmia.—In malarial melanæmia, the capillaries of the brain contain a large number of lymph cells, loaded with black pigment, so that the circulation is impeded. The arterioles may be more or less filled with the same elements, small aneurisms being formed, the walls of which are also pigmented.

Cerebral hæmorrhage.—Cerebral hæmorrhage is sometimes consecutive to blood changes, as in variola, scurvy, leucocythæmia, and is sometimes due to changes in the heart and blood-vessels. Hypertrophy of the heart, coincident with atheromatous induration of the walls of the aorta, internal carotid, and branches of the circle of Willis at the base of the brain, has been regarded as a very frequent cause of cerebral hæmorrhage. It is the fact that atheromatous arteries, having lost their elasticity, can no longer render continuous the intermittent blood-wave projected by each ventricular systole. The jerking impulse of the blood transmitted then into the cerebral capillaries is most probably one of the causes of their dilatation and rupture. But the most frequent lesion which coincides with cerebral hæmorrhage and which may be regarded as its most immediate cause, is aneurismal dilatation of the small arteries and capillaries of the encephalon. Sometimes the capillaries (Pestalozzi and Kölliker), sometimes the arterioles, are the seat of these aneurisms: they have been recently described by Charcot and Bouchard, who consider they play an important part in the pathogenesis of cerebral hæmorrhage (*vide* p. 523).

Two forms of cerebral hæmorrhage may be distinguished—capillary hæmorrhage and focal hæmorrhage.

Capillary hæmorrhage.—The capillary apoplexy of Cruveilhier is seen either in the convolutions or in the central parts of the brain: the portion of the brain affected is softened and scattered over with small red points, which resemble at first sight small drops of coagulated blood. On dissociating the cerebral tissue with needles, these red spots are seen to correspond to blood-vessels, which may be followed and isolated for a certain distance; around them the cerebral tissue is slightly softened, and coloured bright red. On isolating one of these hæmorrhagic spots with its corresponding blood-vessel, and examining it under the microscope, nothing but a mass of blood is at first distinguished; but, by careful washing, a capillary vessel is seen at the centre, the lymphatic sheath of which is distended and filled with blood corpuscles. The red blood corpuscles are also extravasated beyond the perivascular sheath, between the nerve fibres, which are separated and broken. Each one of these small hæmorrhagic foci is thus found to be composed of a blood-vessel, with its perivascular sheath distended with blood, and of a small mass of nervous tissue infiltrated with blood.

Fatty degeneration of the wall of the central capillary is often observed; its perivascular sheath is considerably enlarged, but generally no laceration or fissure can be discovered, through which the blood escaped from the vessel or its sheath, to be infiltrated between the elements of the nervous tissue. These small aneurisms of the perivascular sheath may be cylindrical, fusiform, or spherical, and have been described under the name of *dissecting aneurisms*.

The nerve tubes are broken or dissociated, but, when the capillary hæmorrhage is recent, they have undergone no further degeneration than fragmentation of their myelin. Patients often succumb in the first few days following hæmorrhage; if they su - vive longer, round the vascular dilatations yellow or brown pigment is found, which is free or contained in the lymph cells. These cells also contain fatty granules, which are probably derived from the myelin of the destroyed nerve tubes. The blood contained in the dilated vessels has become brown; blood pigment may also be found in the interior of the vessels and in their perivascular sheaths.

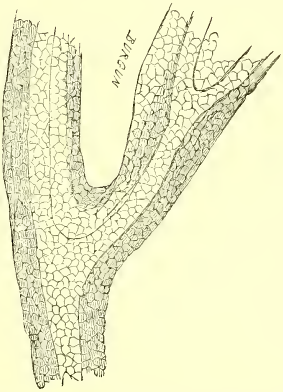

FIG. 269.—CAPILLARY BLOOD-VESSEL OF THE BRAIN AND ITS PERIVASCULAR SHEATH, FILLED WITH RED BLOOD CORPUSCLES, FROM A CASE OF CAPILLARY APOPLEXY.

The small nuclei of old capillary apoplexy are brown or slate-coloured, and are chiefly characterised on microscopic examination by pigmentary changes of the colouring matter of the blood. Brown or black pigment, and even crystals of hæmatoidin, are found in the white blood corpuscles, and in the perivascular sheaths of the arterioles and capillaries. These sheaths, and the peripheral nervous tissue, also contain granular bodies. Simultaneously with these lesions, lacunæ are also found in the brain, about the size of a pin's head, and filled with a transparent fluid. Their walls are more or less stained with blood pigment; they are round or long, and their centre is filled by a blood-vessel the wall of which is infiltrated with fat granules, and the sheath filled with granular bodies.

Hæmorrhagic foci.—A hæmorrhagic focus may be produced by the rupture of a large arteriole, or be the result of the confluence of a large number of capillary hæmorrhagic points; indeed, small capillary hæmorrhagic foci, situated near together, may be so numerous as to form a single focus of considerable size. This view is supported by the fact that around hæmorrhagic foci, even the largest, a certain number of small points or capillary hæmorrhagic foci are found: once formed, a large focus may extend by invading and destroying the neighbouring parts. If situated in the corpus striatum or optic thalamus, it may break into one of the lateral ventricles; if originally seated in the cortical layers of the brain, it may break through the pia mater and arachnoid, and open into the arachnoid space. The most frequent seat of hæmorrhage is the corpus striatum and the optic thalamus, more rarely the white substance of the convolutions. Hæmorrhage may also occur in the cerebellum, the pons varolii, and the medulla oblongata; it is almost always unilateral; sometimes several foci may be found of different ages in various parts of the brain. Large effusions cause tumefaction, with softening of the cerebral tissue, and flattening of the convolutions of the hemisphere affected, so that its existence may be asserted, before cutting into the brain. A hæmorrhagic focus, formed by the rupture of a large vessel, or by the union of many small foci, has the form of a cavity full of blood excavated in the midst of lacerated brain substance; the walls of the focus are simply formed of rugged cerebral substance, stained red with blood.

When the accident has occurred only two or three days before death, the blood is partly coagulated; this is the best time for studying the state of the vessels surrounding the focus, and to ascertain the direct cause of the hæmorrhage. According to the method of Charcot and Bouchard, the focus should then be opened, and together with the surrounding parts of the brain be removed and placed in a vase filled with water, which should be changed with every precaution during the next few days. When the cerebral substance has been sufficiently macerated, it may be washed away by small jets of falling water, the vessels alone remaining. These are then spread upon a glass slide and examined. A ruptured aneurism is often found, belonging, not to a capillary, but to a small arteriole; or miliary aneurisms, which may explain the quantity of blood and the large size of the focus; or, as Charcot and Bouchard have described, a vessel may be found, at the end of which is a ruptured lymphatic sheath, or an artery equally dilated and open, inside which is a fibrinous clot continuous with the coagulum of the focus. By this method the cause of the hæmorrhage may be accurately ascertained.

Miliary aneurisms are most frequently found in the optic thalami, corpora striata, cerebral convolutions, and, finally, in the pia mater. Charcot and Bouchard think that they are preceded by arterio-sclerosis, and particularly by periarteritis, to which morbid process they are due. They insist that hæmorrhage is specially caused by miliary aneurisms and periarteritis, while softening is due more to endarteritis and atheroma; but it must not be forgotten that the lesions of atheromatous periarteritis and endarteritis are most frequently combined. In all cases of spontaneous cerebral hæmorrhage occurring in old persons, miliary aneurisms are found scattered over the cerebral substance, which, by increasing in size, have excavated round spaces in the white or grey matter.

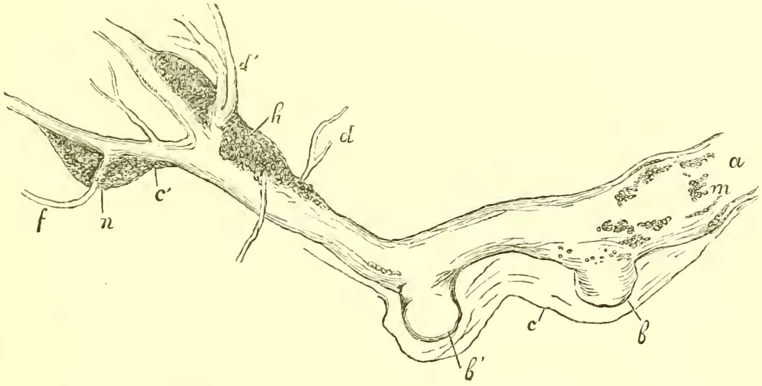

FIG. 270.—MILIARY ANEURISMS OF AN ARTERIOLE OF THE BRAIN.

a, trunk of the arteriole showing the granules *m*; *c*, perivascular sheath; *b*, *b′*, aneurisms formed by an uniform dilatation of the arterial coats; *n*, *h*, effusion of blood into the perivascular sheath *c′*; *d*, *d*, *f*, capillary branches springing from the arteriole. Magnified 30 diameters.

Sequelæ of cerebral hæmorrhage.—If the patient does not die during the first few days following cerebral hæmorrhage, the effused blood undergoes the following changes; the serum exuded from the coagulum is gradually absorbed; the hæmoglobin is changed into yellow and red pigment, and forms crystals of hæmatoidin, and the fibrin breaks down into a granular debris. In the meantime the wall of the focus becomes smoother, a quantity of connective tissue is developed from the elements of the neuroglia, and a true fibrous membrane is formed, which may be found a month after the injury. All the nervous elements contained in the hæmorrhagic focus undergo fatty degeneration, and the myelin is broken up into granules. The formation of a fibrous membrane, inclosing the focus, is the result of the inflammatory process, which is continued till a fibrous cicatrix is produced, in which fatty granules and hæmatoidin are disseminated.

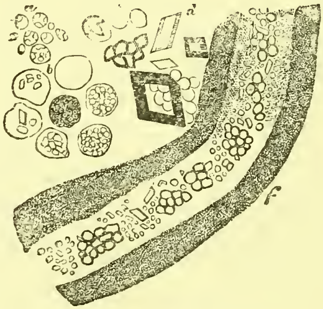

FIG. 271.—CRYSTALS OF HÆMATOIDIN.

a, free crystals ; *b*, crystals contained in cells ; *f*, capillary vessel containing granules of hæmatoidin.

At the end of four or five years the shrunken focus is only represented by a cicatrix, which is often quite colourless, but not unfrequently contains numerous crystals of hæmatoidin. Sometimes, however, cicatrisation is not complete, and in the place of the old hæmorrhagic focus a cyst is found, filled with citron-coloured fluid, and bounded by a fibrous membrane. These cysts are difficult to differentiate from similar cysts produced by softening, the mode of formation of which will be described later. In the majority of cases the cerebral tissue, surrounding a hæmorrhagic focus, undergoes a series of changes, consisting in the infiltration of the colouring matter of the blood between the nervous elements and into the perivascular sheaths. The latter then contain deformed red blood corpuscles, granules, and crystals of hæmatoidin, which are generally found in the lymph cells. It is to the presence of these granules that the nervous tissue round about a hæmorrhagic focus owes its ochrous colour; this coloured zone is opaque, owing to the number of granular bodies contained in the perivascular sheaths; the granular bodies may also contain pigment granules; these bodies are indeed nothing more than lymph cells loaded with fat granules derived from destroyed nervous elements.

Cerebral softening.—Cerebral softening is caused either by embolism, or by arterial thrombosis, following atheroma.

Embolic softening.—Hemiplegia may often suddenly occur in the course of articular rheumatism accompanied with cardiac lesions, or in consequence of atheromatous degeneration of large blood-vessels. This accident is caused by the obstruction of one of the vessels of the brain by a fibrinous clot, which was originally formed in the diseased heart or large vessels. The left Sylvian artery is the cerebral artery most frequently obstructed. The first phenomenon observed is blood stasis in the part of the brain supplied by the obstructed artery, followed by more or less rapid fatty degeneration of the nerve cells and tubes.

In one form the elements simply slowly undergo fatty degeneration. The myelin of the nerve tubes becomes segmented, and transformed into fine fat droplets; the nerve cells break down into a granular debris and disappear. The cells of the neuroglia become filled with fat granules, and changed into granular bodies. We have already seen that all granular bodies are derived from living cellular elements, especially white blood corpuscles, which have absorbed fat granules, and that a nucleus can always be discovered on treating them with picrocarminate of ammonia. Finally, in the vessels filled with coagulated blood and fibrin the pigment separates and the fibrin becomes granular, leaving the vessels full of fat granules and blood pigment. The repletion of the vessels explains how at the commencement of this process the morbid part is tumefied, and projects, if situated on the surface of the brain. Soon, however, the altered elements undergo retrogressive changes, and the infarctus dries, and gradually flattens. The liberated fat often undergoes changes, resulting in the formation of margarin and stearic acid, which are found in the form of round bodies, resembling granular bodies by their opacity, but which, when examined under a high power, appear to be formed of a multitude of acicular crystals united together. The cerebral pulp, which is thus dried and flattened, is yellowish-white, opaque, and firm; but this solidity is only apparent, for it is easily dissociated by a falling stream of water. This form is particularly met with in infarctuses which are seated near the surface of the brain, and dip down into the cerebral substance.

A second form is characterised by pulpy softening of the centre of the infarctus, which is particularly observed in the white substance of the brain. The centre of the infarctus softens more and more, and is finally transformed into a white fluid mass like chalk and water. This fluid is contained in a cavity limited by irregular downy walls, the ragged shreds of which, composed of the debris of blood-vessels which have resisted degeneration, float freely in the cavity. On examining the walls of this focus of softening, only the debris of nerve elements and granular bodies are found. The vessels themselves are covered with fat granules, which can be washed away by agitating the shreds in water, when the following changes may be observed in the blood-vessels: they are empty or filled with a yellowish granular mass; they sometimes still contain blood; their perivascular sheath is dilated, generally irregularly so, sometimes in the form of a crumpled sack; inside it are cells loaded with pigment and fat granules—granular bodies, and endothelial cells, adherent or partly detached, which also contain a few fat granules.

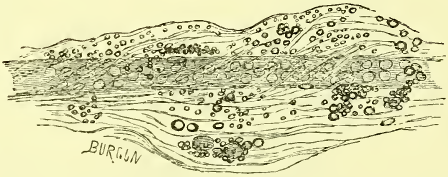

FIG. 272.—CAPILLARY BLOOD-VESSEL IN A FOCUS OF CEREBRAL SOFTENING.

The granular bodies which covered it have been partly removed with a camel's-hair brush, and only a few fat granules are seen ranged round nuclei in the extremely distended perivascular sheath.

These foci of softening may cicatrise by a process similar to that described in apoplectic foci: part of the fluid is absorbed, the elements of the neuroglia surrounding the focus proliferate and soon constitute a thick limiting membrane, containing many blood-vessels. After the lapse of one or two years a cyst filled with serous transparent fluid can only be found, the wall of which does not contain any marked amount of blood pigment, a fact which differentiates such a cyst from that produced by an apoplectic focus.

Infarctuses, occupying only the surface of the convolutions, undergo similar but less marked changes. They soften and are changed into a soft diffluent patch of a peculiar yellow colour, which might be thought to be due to the presence of hæmatoidin, although no trace of it can be found. These yellow patches can be completely dissociated by a stream of water. They are sometimes very extensive, and may occupy the whole surface of a lobe. Again these patches may dry, flatten, and form what appears at first sight to be hard plates; but their firmness is only apparent, for, like the preceding, they may be dissociated by a stream of water. The cerebral convolutions in which this lesion is found are simply wrinkled, flattened, and yellowish, but their general shape is unmodified.

Softening from atheroma and arterial thrombosis.—This is generally the result of atheromatous change in the blood-vessels, a change commencing most frequently in the arteries at the base of the brain. Endarteritis first causes narrowing of the lumen of these vessels, and is followed by blood stasis, which in its turn produces necrosis of the nervous elements. Sometimes irregularities in the internal surface of atheromatous arteries lead to the formation of blood clots which obstruct the circulation; such may occur, for example, in chronic or acute endarteritis of one of the arteries at the base of the brain, chiefly the Sylvian artery, when vegetations may project into its lumen, impede the circulation, and become the starting-point for the formation of a coagulum plugging the vessel entirely. The subsequent lesions of the brain tissue are identical to those produced by embolism. The infarcts produced by thrombosis cause a pinkish coloured softening when the lesion is recent, and soft or hard yellow patches, dried and flattened, when older. When the convolutions are affected and the lesion dates back several months, they are seen to be extremely atrophied, though their general shape is preserved. The pia mater covering them is œdematous, and fills up the hiatus produced by the atrophy. In the central parts of the brain an infarctus due to atheroma, such as embolic infarctus, softens, and forms a fluid resembling chalk and water. The histological lesions are the same in both cases.

Encephalitis.—Encephalitis, or inflammation of the brain, may be diffused or circumscribed: the latter form is related to abscess. Sometimes the cerebral tissue is red, when the change has been described as *red inflammatory softening*, especially by Rostan and Andral; at other times it is yellow, on account of the quantity of pus cells present: such is the so-called *white* or *yellow softening*. Bouchard and Hayem have made an experimental study of the histological process in inflammation of the brain. They used direct irritation of the brain tissue by means of foreign bodies and chemical substances. They ascertained that in cerebral softening, proliferation of the cellular elements of the neuroglia takes place. It is very probable, however, that some of the new cellular elements are simply white blood corpuscles from the blood-vessels; indeed, they are principally found in the perivascular sheaths, and they form more or less voluminous masses in the nervous tissue. At the same time the nerve elements undergo fatty degeneration. The same lesions are observed in acute primary inflammation, ending either in abscess or softening of the brain. The inflammatory softening may be yellow, white, or red; when red it is due to hæmorrhage into the perivascular sheaths, or to an extremely congested condition. Inflammation of the brain may be subacute. It is this form of encephalitis which is observed on the surface of the convolutions in tubercular meningitis, and diffuse meningo-encephalitis (general paralysis of the insane).

In **tuberculisation of the meninges** the surface of the convolutions, particularly at the base of the brain, is the seat of intense congestion, with proliferation of the neuroglia, resulting in softening of the brain tissue.

Diffuse meningo-encephalitis is characterised by various lesions. First, the pia mater and the blood-vessels of that part of the membrane which dips down into the sulci are thickened by an increase of their elements. On raising the pia mater, it is detached from the brain with difficulty, and morsels of the grey matter, adherent to the walls of the blood-vessels, are torn away with it. As the vessels are the seat of frequent congestion, red and yellow pigment is found in their perivascular sheaths, the result of the destruction of the extravasated red blood corpuscles. Finally changes, consisting in multiplication of the elements of the neuroglia, degeneration of the nervous elements, and softening of the grey matter, take place in the brain substance. These lesions are limited to the cortical layer of the convolutions, which may be easily removed by scraping, the white substance appearing firm and distinct beneath, though it is sometimes thought to be denser than normally, owing to thickening of the neuroglia. The whole surface of the brain is affected in the same manner, and the ependyma lining the ventricles is also altered and thickened. Fine transparent granulations are also frequently visible to the naked eye, on the surface of the ventricular ependyma, especially in the fourth ventricle. These granulations are composed of embryonic elements, supplied by a few blood-vessels. The nerve cells present a series of successive lesions, which have been described by Meschede: they become granular, then pigmented, and finally atrophy.

Under the name of **diffuse congenital encephalitis** Virchow has described a peculiar condition of the brain observed in new-born children. In this lesion the cells of the neuroglia first proliferate and then undergo fatty degeneration; the nervous elements also become granular, an abundant formation of granular bodies resulting, and an actual softening, to which capillary hæmorrhages give a red or pinkish colour. But these facts are not very conclusive, and the appearances may be simply due to the normal condition of the fœtal brain. In new-born children indeed, as well as in old persons, granular bodies will be found on the surface of the blood-vessels of the brain, and in the perivascular sheaths. In badly nourished infants, these granular bodies are much more numerous than usual, as Parrot has pointed out.

Abscess of the brain.—Abscess of the brain occurs in purulent infection, from whatever cause, and in consequence of wounds of the cranium. It may also be consecutive to ostitis or necrosis of the bones of the skull, particularly in tubercular ostitis of the petrous portion of the temporal bone, and in syphilitic necrosis of the frontal bone. Such abscesses are continuous with the purulent focus of the diseased bone, or they are developed near the focus, from which they are, however, separated: for example, the dura mater may remain intact between the abscess of the brain and the diseased bone. Cerebral abscesses are generally small, and are formed in the same way as in other organs; they are either solitary, or disseminated in large numbers throughout the brain. They are characterised by a yellow, ropy, often viscous fluid, which contains mucin, precipitated by acetic acid, and also a large number of cellular elements. This fluid is inclosed in a cavity with downy and irregular walls, in which connective-tissue elements may be developed, ending in the production of fibrous tissue. Sometimes these abscesses may increase in size and open into the arachnoid space, or into one of the ventricles; sometimes they remain as purulent cysts in the substance of the brain.

Chronic encephalitis, or **Sclerosis.**—This lesion, which is often primary in the brain, may also follow a similar lesion begun in the spinal cord. Two distinct periods or degrees must be admitted in its evolution. In the first period, rapid multiplication of the elements of the neuroglia causes the brain tissue to become soft and gelatinous, like all embryonic tissues. The second period is distinguished by atrophy of all the new elements, and by the development around them of numerous and extremely delicate fibres interlacing in every direction; the cerebral tissue is hard and resisting, and, on examining a delicate section of the morbid part under a high power, the fibrils are seen to form a perfect matting, and between them are found atrophied nervous elements, and small cells with a round or oval nucleus. These two stages of the same disease may be found in the same brain.

Idiopathic sclerosis of the cerebrum and cerebellum may be met with in the brains of idiots, cretins, and sometimes of epileptics, in which cases the morbid change is generally localised. Duguet has collected three cases of localised sclerosis of the brain in epileptics at the Salpêtrière. When the lesion affects several cerebral convolutions, some may be swollen, semi-transparent, soft and gelatinous, while others are, on the contrary, small, flattened, and so hard that they can be hardly indented with the finger nail: thus the various stages of sclerosis may be met with in the same brain.

At the beginning of the disease the nerve cells seem to be quite colourless and transparent, and slightly atrophied though preserving their angular form. When the lesion is old and the tissue very hard, the nerve cells and tubes have almost all atrophied, sometimes even they have entirely disappeared. A great number of amyloid corpuscles are generally, in sclerosis of the brain, scattered over the surface of the atrophied convolutions and in their substance. Finally, those lesions which are formed round cerebral tumours, and particularly round large tubercles, are related to sclerosis: they are characterised by the formation of new fibrillar connective tissue, sometimes of considerable thickness.

Tumours of the brain. Sarcoma.—In the brain as well as in the meninges two distinct forms of sarcoma are seen: neurogliac and angiolithic sarcoma (*vide* p. 144).

Fibroma.—Fibroma of the brain is rare. We have had the opportunity of examining one which was located in the white substance of the right crus cerebri. It was about the size of a filbert, extremely hard, and composed of fine undulating fibrils and small uni-nucleated cells.

Lipoma.—A solitary case of lipoma of the brain, part of which was ossified, has been reported by Benjamin.

Carcinoma is rare in the brain, sarcoma is frequently confounded with it.

Papilloma.—We have seen one case of papilloma of considerable size. It was seated upon the ependyma of the third ventricle, projecting into the lateral ventricles through the foramen of Monro. This granulating mass, engorged with milky juice, and surrounded with softened cerebral tissue, might have been mistaken for carcinoma. It was composed of a cauliflower excrescence formed of dilated blood-vessels, lined with pavement cells, which by desquamating gave the fluid its milky appearance.

Tubercle.—Tubercles of the brain form tumours resembling sarcoma in external appearance. Instead of being small, like the tubercles of other organs, they may reach the size of a pea, or even of a doubled fist. Their microscopical characters are generally marked. They are hard, compact, and so intimately connected with the brain tissue that they can only be enucleated with difficulty. On cutting across one of them and the surrounding tissue, its centre is seen to be yellow, and its peripheral layer grey, semi-transparent, and directly continuous with the cerebral tissue. In the cerebral tissue surrounding the tubercle active proliferation of the neuroglia is observed, as well as large multi-nucleated cells and blood-vessels showing tubercular changes. On microscopically examining a blood-vessel of the brain passing

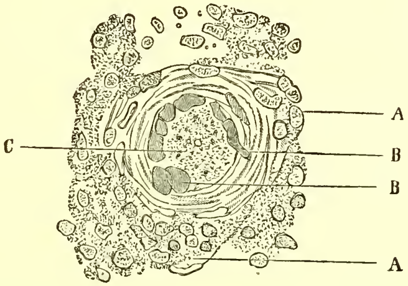

FIG. 273.—SECTION OF A BLOOD-VESSEL IN THE MIDST OF A TUBERCLE OF THE BRAIN.

The lumen of the vessel C is filled with granular fibrin ; B, white blood corpuscles contained in the vessel and clinging to its internal surface ; A, cellular elements contained in the lymph sheath. Magnified 300 diameters.

towards a tubercular mass, its perivascular sheath is found to be filled with a large number of embryonic elements, and this while the vessel is still in the midst of normal nervous elements. When it penetrates the grey and semi-transparent zone of the tubercle, the sheath suddenly dilates and seems triple its original size; once it has reached the caseous zone of the tubercle it becomes blended with it. The vessel itself becomes obliterated by fibrin, throughout its whole course through the tubercular mass.

Though at first sight tubercular masses in the brain seem to be actually single tumours, discrete or confluent tubercles are frequently seen at their margins. On examining delicate sections of cerebral tubercle, cut after hardening in alcohol or chromic acid, the same characters and the same details of structure will be observed as in tubercle of all other organs: small cells imbedded in a granular substance, vessels obliterated by fibrin, granular degeneration of the cerebral elements of the tumour, etc.

Syphilitic gummata.—While gummata of the dura mater are frequent, those of the cerebral substance are rare. They present all the appearances already described as characteristic of gummata in general. They vary in size from that of a pea to that of a nut, in shape they are generally angular, and they are located in the hemispheres, the pons varolii, and the cerebellum. On cutting across them two zones are recognised, one central, opaque, yellow, caseous, and hard, the other peripheral, grey, semi-transparent, and blending with the neighbouring cerebral tissue, which is affected with secondary encephalitis. The cellular elements at the centre of the gumma are small and in a state of fatty degeneration, and the blood-vessels are here partly obliterated. In the semi-transparent zone, branching cells—the cells of Deiters—are found in the midst of an embryonic tissue composed of small round cells, and also blood-vessels with their perivascular sheaths filled with lymph cells.

Neuroma.—Medullated neuromata, that is, composed of nerve cells and neuroglia, have been found on the surface of the brain (*vide* p. 235).

Cysts are chiefly developed in the choroid plexuses: they may be serous and transparent.

CHAPTER XVI.

LESIONS OF THE SPINAL CORD.

I. Normal Histology of the Spinal Cord.

Configuration of the spinal cord.—The spinal cord, situated in the middle of the vertebral canal, is surrounded with membranes similar to those of the brain, namely, the dura mater, the arachnoid, the sub-arachnoid connective tissue, and the pia mater. The cephalo-rachidian fluid is contained in the sub-arachnoid tissue. The spinal marrow is elongated in the form of an almost cylindrical cord, and presents two enlargements, the cervical and the lumbar enlargement; it ends in a cone at its lower extremity, where it is continuous with the filum terminale. The pia mater, which is very thick, adheres closely to the cord; beneath this membrane may be distinguished, on the surface of the cord, several longitudinal fissures, the anterior median fissure, the posterior median fissure, and the lateral fissures from which the anterior and posterior nerves spring. These nerves on emergence from the spinal cord unite to pass through the vertebral notches; the posterior, after emerging from the dura mater, are connected with the spinal ganglia; they are much larger than the anterior. The anterior and posterior fissures divide the spinal cord into two symmetrical halves, united by a commissure. The white tract of the spinal cord, contained between the anterior fissure and the anterior roots, is called the anterior column, and the tract between the posterior median fissure and the posterior roots is called the posterior column; the lateral columns comprise all that part of the white cortex of the cord lying between the anterior roots in front and the posterior roots behind. On dividing the spinal cord transversely it is seen to be composed of a peripheral white substance, and of a central grey substance; the latter has somewhat the form of the letter H, the two anterior branches forming the anterior horns, and the posterior, the posterior horns, the horizontal line representing the grey commissure.

Structure of the spinal cord.—The white cortex of the spinal cord, which forms the anterior, lateral, and posterior columns, is largely composed of medullated nerve fibres, passing in a longitudinal direction; thus, in their transverse section, they appear as small circles, in the centre of which is seen a section of the axis cylinder. Oblique and horizontal fibres are found in the white commissure, in the lateral columns, and in the posterior columns, near to the posterior cornua, at the spots where the nerves emerge.[1]

The grey matter of the anterior and posterior cornua contains a large number of nerve cells, the arrangement and shape of which differ according to the parts of these cornua under examination. The nerve cells of the anterior cornua, called motor cells, because of the important function they exercise, are very large, so large indeed that they may be distinguished with the naked eye, when stained and isolated. They have a great number of ramifying or protoplasmic processes, and one process which does not ramify, called the axis cylinder, or Deiters' process (*vide a*, fig. 20, p. 30). They form distinct groups in the cord, particularly in the cervical and lumbar enlargements. The cells located in the most anterior part of the anterior cornua are divided into two groups, an antero-internal, and an antero-external; the latter is again, at the lumbar and cervical enlargements, separated into several distinct groups. At the angle projecting outwards, which is seen at the posterior part of the anterior cornua, there is another group of smaller cells. The columns of Clarke (the dorsal nuclei of Stilling), which are situated at the union of the anterior and posterior cornua, contain a rather considerable number of nerve cells of medium size. The posterior cornua, and the gelatinous substance of Rolando, contain much smaller nerve cells, most of which are fusiform with two or three processes. The posterior cornua decrease in size as they pass directly into the posterior roots, while the anterior cornua do not reach the cortex of the cord. The sensory roots penetrate the posterior cornua, partly passing through the substantia gelatinosa, where they form small separate fasciculi.

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[1] In order to study the spinal cord, either in the normal or pathological state, its different elements must be first examined, namely the cells of the anterior and posterior cornua, and the nerve-tubes, either by dissociating them in the fresh state, or after they have been acted upon by colouring reagents—carmine, picro-carminate of ammonia, or osmic acid. Examination in the fresh state must be supplemented by study of sections of the spinal cord, but there are elements which can only be well seen in the fresh state, such as, for example, cells in the condition of fatty degeneration, and granular bodies; but on the other hand the arrangement of the elements, their grouping, their pathological changes, such as atrophy of certain groups of cells or fasciculi, more particularly sclerosis, or hypertrophy of the connective tissue of the spinal cord, can only be exactly appreciated in sections. These are generally cut horizontally. Previous hardening of the spinal cord is necessary, to obtain which various methods are employed: either immersion in a ·2 per cent. solution of chromic acid, which should be changed frequently, or in Müller's fluid or bichromate of potash or bichromate of ammonia, or first in alcohol for twenty-four hours followed by the action of chromic acid and the bichromates. Two or three months at least are necessary to obtain complete hardening. Delicate sections may be then cut, stained with carmine or picro-carminate, rendered transparent by the successive action of alcohol and the essence of turpentine or cloves, and preserved in Canada balsam or Damar resin.

The grey commissure, situated behind the white commissure, is pierced in its centre, by the canal of the ependyma, which is continuous above with the fourth ventricle, and below with the filum terminale. The cavity of this canal, which is generally obliterated, is lined with a layer of cylindrical cells; on each side of it are seen two large arterial and venous trunks, behind it is the posterior commissure of grey matter, traversed by a few nerve fibres, passing in a transverse direction.

The connective tissue of the neuroglia is continuous with the pia mater, and supports the blood-vessels which ramify from the circumference to the centre; it also surrounds all the nerve tubes of the white columnus. It is rather abundant in the grey substance of the cornua, as well as in the posterior commissure, around the central canal, and near the posterior median fissure. It is essentially composed of delicate and extremely long fibres, though it also contains flat or round cells, which are particularly numerous in the grey matter.

The longitudinal white tract of the cortex of the spinal cord may be divided, as we have already said, into anterior, lateral, and posterior columns, each one of these columns being also divided into two secondary fasciculi: for example, anterior internal and anterior external fasciculi, anterior lateral and posterior lateral fasciculi, are distinguished. This division, which is a little arbitrary, is only visible externally in the posterior columns, which are separated into two fasciculi by the intermediate posterior fissure. The fasciculus comprised between the posterior median fissure and the intermediate fissure is called the column of Goll, and that between this fissure and the posterior root the cuneiform column; the latter, which is adjacent to the posterior cornua, and which is traversed by the fibres of the posterior roots, is also called the posterior radicular zone.

Probable course of the fibres of the spinal cord.—Though the structure of isolated elements of the spinal cord, nerve tubes, and cells is at present tolerably well known, little is understood regarding their reciprocal relations, and we are reduced to more or less rational hypotheses based on physiological and pathological data. It is known that each nerve cell of the anterior cornua is connected with a nerve tube of the anterior roots by the process of Deiters, and that the numerous ramifying processes which spring from nerve cells are either lost in the tissue of the neuroglia or anastomose with processes proceeding from neighbouring cells. The white fasciculi of the antero-lateral columns are considered to be the receivers of motor impulses emanating from the brain and the anterior cornua of the spinal cord. The posterior roots are connected with the posterior cornua; their most external fibres pass between the longitudinal fibres to enter the grey matter, then traverse the substantia gelatinosa, and bend round to take a vertical direction in the posterior columns. They may also be inflected to pass to the anterior part of the posterior cornua, or even into the anterior cornua. The internal fibres of the posterior roots curve over in the shape of an arc or *s*, and take a horizontal direction across the external portion of the posterior columns, and penetrate the anterior part of the posterior cornua, or are lost in the anterior cornua; they doubtless terminate in the cells of the columns of Clarke. On examining the spinal cord, from the cervical to the lumbar region, the white fasciculi are seen to diminish in thickness, in comparison with the grey matter; they are, in fact, reinforced from below upwards, by the nerves proceeding partly to the grey centres of the spinal cord, and partly to the cerebrum and cerebellum.

II. Histological Lesions of the Spinal Meninges.

Although most of the facts described regarding the cerebral meninges are also applicable to the membranes of the spinal cord, yet since certain lesions of the latter are not found in the former, or differ from them greatly, we have thought it well to devote a special description to lesions of the spinal meninges.

Hæmorrhage into the spinal meninges.—More or less considerable effusions of blood may occur, either round the dura mater, or between this membrane and the osseous canal, or into the arachnoid cavity, or the sub-arachnoid spaces. In the first case the blood is diffused and partly coagulated in the cellulo-adipose tissue, and round the roots of the nerves. In the second, it exists either as small ecchymoses on the internal surface of the dura mater, or as an actual effusion of blood varying in extent. These hæmorrhages are due, either to direct or indirect wounds, lesions of the blood-vessels, and sometimes even to aneurisms. They are also met with in tetanus, asphyxia, and meningitis.

Meningitis.—Acute meningitis and epidemic cerebro-spinal meningitis have been already described on page 579. Chronic spinal meningitis, which differs in a marked manner from cerebral meningitis, will, however, be described here. Chronic spinal meningitis is not rare; it may affect either the dura mater, the arachnoid, or the pia mater. Chronic pachymeningitis is met with whenever inflammatory or other tumours, springing from the vertebræ or the vertebral articulations, project into the vertebral canal, and cause irritation of the dura mater. There are two forms of chronic pachymeningitis, which should be treated separately: hypertrophic cervical pachymeningitis, and tubercular meningitis, or Pott's disease.

Hypertrophic cervical pachymeningitis.—This very rare lesion, which had been merely indicated by many authors, was first fully described by Charcot and Joffroy ('Archives de Physiologie,' 1869). In this disease the cervical spinal cord and its membranes form a fusiform enlargement, which fills the vertebral canal, and adheres to the vertebral ligaments. The meninges, thickened and adherent together, form, with the spinal cord which they surround, a mass in which the component structures cannot be separated from one another. In a transverse section, passing through the whole tumour, the dura mater is found considerably thickened, measuring several millimetres in diameter. When the line of demarcation between the dura mater and the pia mater is still visible, the latter is seen to be thickened in a very marked manner. In the deformed spinal cord, flattened from before backwards, the white and grey substance can sometimes be tolerably distinctly recognised.

Microscopical examination of the dura mater shows that it is composed of a great number of laminæ of connective tissue, arranged in concentric layers, resembling in structure the cornea, or lamellar fibroma. The nerve fibres of the roots passing through the diseased dura mater are more or less compressed and altered. In the midst of this envelope of fibrous tissue, formed in a great part by the dura mater, the spinal cord itself is found to have undergone great changes: the white substance, for example, may be sclerosed and have become grey and semi-transparent, so that it is hardly possible to differentiate it from the central grey matter. Histological study of the sclerosed part of the white substance shows all the lesions of sclerosis of the spinal cord, described later; if, in some parts of the spinal cord, islets of grey and white matter may be found, elsewhere the lesions are more pronounced. This more or less extensive partial destruction of the cervical spinal cord determines secondary degeneration below and above the diseased part, which is ascending in the posterior columns and descending in the anterior columns.

Chronic tubercular pachymeningitis, or Pott's disease.—In most of the cases of Pott's disease, accompanied with tubercular ostitis or fungoid arthritis, the dura mater is more or less affected; it is rare for it not to be thickened and covered externally, at the level of the diseased vertebræ, by a thick layer of caseous pus. Its external surface is generally covered with fungoid granulations of a dirty grey colour, and infiltrated with caseous pus (*external caseous pachymeningitis*). The anterior vertebral ligament is dissociated and destroyed in parts, so that the pus passes from the vertebræ, and that which is secreted on the surface of the dura mater burrows between the external surface of the dura mater and the osseous canal, and often communicates directly with a sac full of pus, which projects in front of the vertebral column, beneath the common anterior vertebral ligament. Inflammation of the dura mater is limited exactly to the parts of the vertebra diseased. The membrane is infiltrated either in its external layers alone, or throughout its whole thickness, by numerous embryonic cells. When affected throughout its whole thickness, its internal surface, which is in contact with the arachnoid and pia mater, also shows manifest signs of inflammation: Vulpian has seen new vascular false membranes produced. Michaud,[1] who made a histological study of pachymeningitis, has seen the deep layers of the dura mater infiltrated with embryonic elements between the fibrous fasciculi and laminæ, while prominent granulations on its external surface were filled with the same elements compressed into a thick layer and infiltrated with fat granules: he has also noticed in the substance of these new formations small foci, containing round cells in a condition of fatty degeneration, and which he regarded as microscopic purulent foci. One of us, having observed many of these facts, has found tubercular granulations in different stages of evolution in the thickened dura mater, and in the caseous granulations on its external, and even on its internal, surface. These granulations, which are very characteristic, are discrete or confluent, and contain numerous giant cells,[1] a certain number of which undergo caseous melting. It is probable that in most cases of caseous pachymeningitis, related to Pott's disease, the disease must be attributed to tubercular inflammation of the dura mater.

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[1] *De la méningite et de la myélite dans le mal vertébral.* Thèse de doctorat.

Consecutive to these lesions of the vertebræ, dura mater, arachnoid, and pia mater, the spinal cord and nerves are altered to a variable degree ; sometimes, however, the spinal cord may entirely escape morbid change. The pathological changes of the spinal cord and nerves are not solely due to compression, but generally to the extension of inflammation. The spinal cord is often softened, diffluent, or converted into an atrophied yellowish mass, in which the grey cornua and white columns can no longer be distinguished; it is also infiltrated with numerous granular bodies.

Michaud and Charcot have reported a case in which a patient, originally paralytic in consequence of Pott's disease, recovered from paraplegia so as to be able to walk. The autopsy showed partial atrophy of the spinal cord, which was reduced to a fifth of its normal size, and sclerosis of the white substance, only one of the anterior cornua remaining. The nerve fibres which were preserved showed no change. The authors supposed that these nerve fibres were regenerated nerve tubes, but this was not proved. It might be thought that the spinal cord, filled at first with the products of degeneration, such as granular bodies, and unable to perform its functions on account of their presence, resumes its activity when these inflammatory products have been reabsorbed. Masius and Van Lair have observed regeneration of the spinal cord and recovery of its functions in frogs, not only after simple section, but also after ablation of a portion of this organ. At the end of a few months they found in the grey tissue interposed between the two portions of the divided spinal cord, bi-polar and multi-polar cells, regarded by them as nerve cells, and fibres described as fibres of Remak. If however experiments on frogs have given positive results, those which have been performed on mammals have hitherto given negative results. An opinion cannot yet be formulated on the regeneration of nerve elements in the spinal cord in man, in cases of atrophy following the myelitis of Pott's disease.

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[1] In the first case presented by one of us to the Société de Biologie (*Comptes Rendus*, 1873, p. 263), there were in the midst of the dura mater cavities filled with rather large epithelioid cells. These cavities had previously been mistaken for sections of inflamed lymph vessels. Later, we had the opportunity of examining many other cases of pachymeningitis, in which the granulations and thickened embryonic tissue of the dura mater also showed very characteristic tubercle. On examining then again the sections of the dura mater made from our first case, we easily recognised that the cavities, which we had regarded as sections of lymphatics, were nothing more than masses of epithelial and giant cells, such as are found in tubercle.

Chronic spinal meningitis, characterised by more or less considerable thickening of the pia mater, and adhesion of the two layers of the arachnoid, is particularly observed, after chronic affections of the spinal cord, softening, or sclerosis. Thus, in sclerosis of the posterior or lateral columns, the pia mater is chronically inflamed at the level of the diseased parts of the cord.

On opening the spinal cord of old persons, **fibrous** or **calcareous plates** are frequently unexpectedly found in the arachnoid; they are seated generally in the posterior and inferior part of the cord, near the cauda equina; the visceral layer of the arachnoid is the most frequently affected. These plates, varying in length from a half to two centimetres, may be rather numerous, and are composed of fibrous tissue generally calcified. They are slightly transparent, and resemble cartilaginous tissue; they, however, never contain cartilage cells; they sometimes undergo a kind of ossification, that is to say, that in the midst of the calcified connective tissue may be found lacunæ furnished with canaliculated processes, inclosing a small elongated cell: it might be concluded that these were bone corpuscles; but the tissue is not vascular, and contains no Haversian canals. In two cases published by Jaccoud and Vulpian, these plates seem to have caused accidents which were referred to pressure on the spinal roots; but in most cases in which they are found at the autopsy they have caused no appreciable symptoms during life.

III. The Pathological Histology of the Spinal Cord.

Recent and numerous researches on the spinal cord have thrown light on a series of diseases of the nervous system which were formerly obscure, or were regarded as simple neuroses. Pathological lesions and their connection with the symptoms observed are better understood in the spinal cord than in the brain or sympathetic system, which is due to the fact that the structure and physiology of the spinal cord are better understood than in the case of the encephalon. In the scientific progress of recent years the researches of French physicians, particularly Duchenne of Boulogue, Charcot, Vulpian, and their pupils, have without doubt greatly advanced our knowledge of the lesions of the nervous system, and in this treatise we propose to profit largely by their researches.

The pathological histology of the spinal cord differs little from that of the brain, and is in reality extremely simple. It includes nutritive modifications of the nerve cells, their hypertrophy, atrophy, and pigmentation, and even their complete disappearance in consequence of insufficient nutrition, a not unfrequent consequence of chronic inflammation; also similar lesion of the nerve tubes, which, in recent myelitis, sometimes show atrophy of their axis cylinders, and at the same time nutritive lesions of the myelin, which we have already studied when considering division of the nerves. Later the myelin may completely disappear, but the axis cylinders exist much longer, sometimes even indefinitely, although atrophied. Simultaneously with changes in the elements of the nervous tissue, the connective tissue of the neuroglia undergoes parallel modifications; such as, in acute processes, tumefaction of the flat cells of the neuroglia, and the new formation of small round elements or lymph cells, and granular bodies. Later, in chronic processes, either inflammatory or degenerative, the fibrous tissue and neuroglia thicken, and the nerve tubes, or rather the axis cylinders left after the total disappearance of the myelin, become surrounded with numerous fibrils thicker than normal. This change constitutes what is called by the name of sclerosis.

Sclerosis ends in making the tissue of the organ much denser, and in atrophy of the nerve elements, the functions of which are abolished. It is not produced suddenly, for it is the consequence of acute or subacute inflammation, which first affects either the grey centres or the white fasciculi of the spinal cord or brain. In all cases of sclerosis, as well as in atrophy from whatever cause, and in all chronic processes, the spinal cord, particularly its peripheral layers and the fibrous tissue surrounding the central canal, contain a considerable quantity of amyloid corpuscles. They are small, spherical bodies, vitreous and refractive, and stain violet with a solution of iodine; it is owing to this reaction that they have been called amyloid, though they are formed of a proteid substance, the chemical composition of which differs entirely from starch. Simultaneously with these lesions of the elements of the nervous tissue and neuroglia, the blood-vessels show changes already considered, congestion, exudation, granular bodies, etc. These two series of nutritive and inflammatory troubles, some affecting the nerve cells and tubes, others the connective tissue, though most frequently united, may nevertheless be referred, the former to parenchymatous inflammation, the latter to interstitial inflammation. But interstitial inflammation, or sclerosis, is rarely primary ; it more often follows lesions of the trophic centres, either in the spinal cord or in the encephalon.

Affections of the spinal cord, reduced to degenerative or inflammatory processes, the histology of which is simple, would not furnish subjects for so many investigations, did not the most elementary lesions, carefully studied, furnish data for general deductions. To describe lesions corresponding to the different diseases of the spinal cord, which have been defined for the last twenty years by their symptoms, as well as by their pathological anatomy, we should have to enter into fuller details regarding the topographical pathological anatomy of the spinal cord.

We have already, on page 601, briefly described the various columns of white substance, and the masses of grey matter. These data, borrowed from descriptive anatomy, are useful at each step in the pathology of the spinal cord ; in fact, most of the diseases of the spinal cord are essentially and originally localised in some one of the columns of white substance or grey substance, and most frequently throughout the whole length of the cord. In locomotor ataxy, for example, the primary seat of the disease is in the posterior radicular columns (Pierret) or cuneiform columns, implicating later the columns of Goll, that is to say, affecting the whole of the posterior columns. Such is again peri-ependymar myelitis, limited to the connective tissue surrounding the central canal (Hallopeau) ; such are infantile paralysis, spinal paralysis of the adult, progressive muscular atrophy, which diseases, though distinguished from each other by their symptoms and duration, have none the less a common point of origin in an acute or subacute inflammatory lesion ending in atrophy of the grey anterior cornua (*acute or subacute anterior poliomyelitis*) ; such is, again, amyotrophic lateral sclerosis (Charcot and Gombault), shown by the symptoms of spasmodic paraplegia.

Degenerative myelitis, consecutive either to localised destruction of the spinal cord in a transverse direction, as may occur in

Pott's disease and tumours, or to foci of softening or apoplexy in the brain, always takes a longitudinal course in the spinal columns. Most of the primary or secondary diseases of the spinal cord may be included in a group of *systematic lesions*, according to Vulpian's expression. They are invariably localised in certain fixed columns, without implicating adjacent parts of the cord. In opposition to systematic lesions, other lesions of the spinal cord are called *diffuse*. In spite of the progress effected during the last thirty years in cerebral and spinal pathology, it must not be thought that the lesion of every nervous affection has been determined. Hysteria, true epilepsy, paralysis agitans, have not yet been referred to any persistent lesion of the nervous tissue, nor in tetanus and hydrophobia can any constant lesions be always recognised after death.

With these preliminary remarks we shall now proceed to examine successively the various lesions of the spinal cord.

Congestion.—Congestion of the spinal cord is seen simultaneously with congestion and inflammation of the meninges, in typhoid fever, certain forms of rheumatism, febrile diseases, and in chronic cardiac disease. It is characterised by distension of the blood-vessels. Schröder van der Kolk has advanced the opinion that the medulla oblongata is congested in every case of epilepsy, but this opinion has not been confirmed. In post-mortem examinations it is very difficult to say if the fulness of the blood-vessels and staining of the spinal tissue are due to the position of the body after death, to cadaveric stasis, or to hyperæmia which existed during life. Congestion can only be positively affirmed when blood pigment is found round the vessels, in the perivascular sheaths, or in the spinal tissue.

Spinal hæmorrhage, or Hæmatomyelia.—Hæmorrhage into the spinal cord is rare; it is seen either as an infiltration of blood, or as an isolated blood clot in the midst of dissociated and destroyed spinal tissue; it is generally seated in the grey centres of the cord, and may extend for a considerable distance. The lesions of the blood-vessels, the ultimate changes of the clot and nervous tissue, are similar to those already described in cerebral apoplexy. According to Charcot and Hayem, this accident is always consecutive to myelitis, of which it constitutes a peculiar form—apoplectiform myelitis. It may also be the result of sudden variations of barometric pressure on the spinal cord. In animals subjected by

M. Bert to high atmospheric pressure, which was suddenly relaxed, the expansion of gases contained in the blood produced lacerations of the blood-vessels of the spinal cord, and even sudden death by capillary hæmorrhage and laceration of the nervous tissue. The same causes sometimes produce the same effects in man.

Softening.—Softening, consequent on arterial embolism and atheroma of the blood-vessels of the cord, is very rare; the lesion is localised in a limited region of the organ. The colour, consistence, and structure of the softened part vary exactly in the same way as in cerebral softening, already described. Sometimes the softened part is soft, diffluent, whitish, and opaque, and yields a milky fluid on section; at other times the altered part is, on the contrary, dry, yellow, shrunken, and atrophied. On letting a stream of water fall upon it, however, this hardness is seen to be only apparent; the water carries away the dissociated elements, which give it a milky opacity. On examining fresh specimens under the microscope a considerable number of granular bodies, derived from the granular destruction of the myelin of the nerve tubes, is found in both cases, as well as altered blood-vessels, the perivascular sheaths of which are full of the same morbid elements.

Softening of the spinal cord is very frequently observed in compression of this organ by a tumour located in the spinal meninges. In such a case, two series of lesions must be distinguished: the first consists in a focus of softening, or in diffused inflammation, related to vertebral caries or tubercular pachymeningitis; the second is characterised by secondary degenerations above and below the diseased point. These secondary degenerations, some ascending in the columns of Goll, others descending in the pyramidal fasciculi, are constant, whatever may be the nature of the lesion producing the transverse solution of continuity in the spinal cord. They are extremely interesting, for they assist us in determining the course of the fibres of the spinal cord, and the physiological function of the white columns, and also in explaining and interpreting the motor and sensory symptoms observed in Pott's disease. Similar degeneration of the antero-lateral fasciculi result from lesions of the brain, for example, when hæmorrhage or softening has destroyed a large part of one of the cerebral hemispheres.

Secondary degenerations of the spinal cord.—The parts of the spinal cord which are altered, either in consequence of a destructive lesion or focus in the brain or cord, show changes resembling those of myelitis. Sometimes the affected parts appear normal to the naked eye; at other times they are more opaque, which is due to the great number of granular bodies present, or they are semi-transparent, owing to the absorption and disappearance of the myelin. The diseased spinal tissue is generally rather softened, though it may be condensed; the altered fasciculi are usually much atrophied. Examined under the microscope in the fresh state, granular bodies are generally seen to be present in great numbers. In sections hardened with chromic acid, Müller's fluid, or the bichromates, stained with carmine, cleared with turpentine, and mounted in Canada balsam, the granular bodies are no longer visible, but the lesions of chronic sclerosis can always be distinguished by this method. The nerve tubes are seen to be atrophied and deprived of their myelin, though the axis cylinders are still preserved. The degenerated fasciculi first show the appearances of myelitis with softening, then those of sclerosis.

We will proceed now to examine each case in particular, with special regard to the seat of the lesion.

Secondary degeneration of the spinal cord, consecutive to an apoplectic focus or to softening of the brain.—It is necessary to recall here the cerebral origin of the pyramidal fasciculi, their course in the brain, pons varolii, and medulla oblongata, and their termination in the spinal cord. Taking the pyramidal fasciculi in the medulla oblongata, where they form the anterior pyramids, and following them as they pass upwards into the brain, they are found to pass under the transverse fibres, intersect with those of the pons, and to be collected again into a distinct fasciculus, in the lower plane of the crus cerebri. According to the researches of Flechsig, they occupy the middle third of the inferior stage of the crus; they then, with the cerebral expansion of the crus, penetrate the internal capsule between the optic thalamus and corpus striatum, pass upwards into the centrum ovale, and from there into the cerebral convolutions. According to Flechsig and Pitres, the pyramidal fasciculus passes through the posterior part of the internal capsule, to end in the frontal and ascending parietal convolutions and the paracentral lobule, which convolutions border the fissure of Rolando (the psycho-motor centres of the limbs). To return now to the medulla oblongata, where the pyramids decussate before descending into the spinal cord. This decussation of the pyramids takes place in the three following ways: First, the most frequent is, that the pyramid divides into two fasciculi, one direct, which descends in the anterior column of the cord of the same side, and the other larger, which decussates with the opposite fasciculus, and passes into the lateral column of the cord on the opposite side. This decussated pyramidal fasciculus is, in a transverse section of the spinal cord, found in the most posterior part of the lateral column, in contact with the posterior roots. The relative sizes of the direct and decussated fasciculi vary; the latter may be extremely small, thus explaining direct paralysis of cerebral origin, which is, however, extremely rare. Secondly, in one person in six, decussation is complete and there is no direct fasciculus. Thirdly, one only of the pyramids may divide into direct and decussating fasciculi, the second pyramid crossing in its entirety. Thus, in the spinal cord, the fasciculi of the pyramids usually occupy two distinct regions: the direct fasciculus (A′, fig. 274) is situated at the most internal part of the anterior column, alongside the anterior median fissure; the decussated fasciculus (A, fig. 274), or Türck's fasciculus, is larger, and is situated at the most posterior part of the lateral column, in contact with the posterior cornua, never extending, however, as far as the cortex of the cord, the surface of

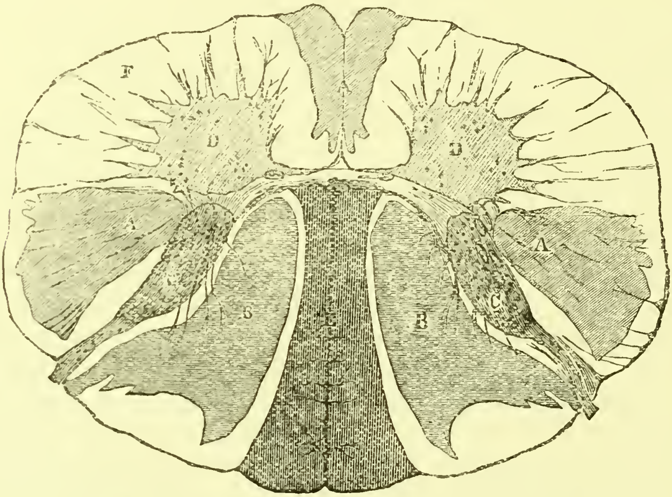

FIG. 274 —TRANSVERSE SECTION OF THE CERVICAL ENLARGEMENT OF THE SPINAL CORD. (AFTER CHARCOT.)

A′, A′, direct anterior fasciculi; A, A, the decussated pyramid fasciculi or Türck's fasciculi; B, B, posterior radicular zones; C′, C′, posterior cornua; D, D, anterior cornua; F, anterior radicular zones; E, columns of Goll.

the lateral column being bordered by the direct cerebellar fasciculus. The pyramidal fasciculi appear to be lost in the anterior cornua of the cord.

These data result from researches on the development of the pyramidal fasciculi, which in new-born infants are sooner provided with medullary sheaths than the neighbouring parts.

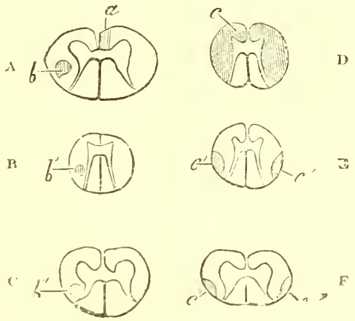

FIG. 275.—SECONDARY DEGENERATION OF THE SPINAL CORD.

The three figures A, B, and C represent a case of old lesion of the right hemisphere. The shaded parts indicated the seat of the secondary degeneration; *a*, altered direct fasciculus; *b*, seat of the lesion in the left lateral fasciculus in the cervical region of the cord; *b'*, the same lesion in the dorsal region; *b''*, the same lesion in the lumbar enlargement. The figures D, E, F show sections of the spinal cord in the dorsal and lumbar regions, below the spot where the cord has been entirely destroyed by compression. The shaded parts *c*, *c'*, and *c''* represent the seat and extent of the descending degeneration.

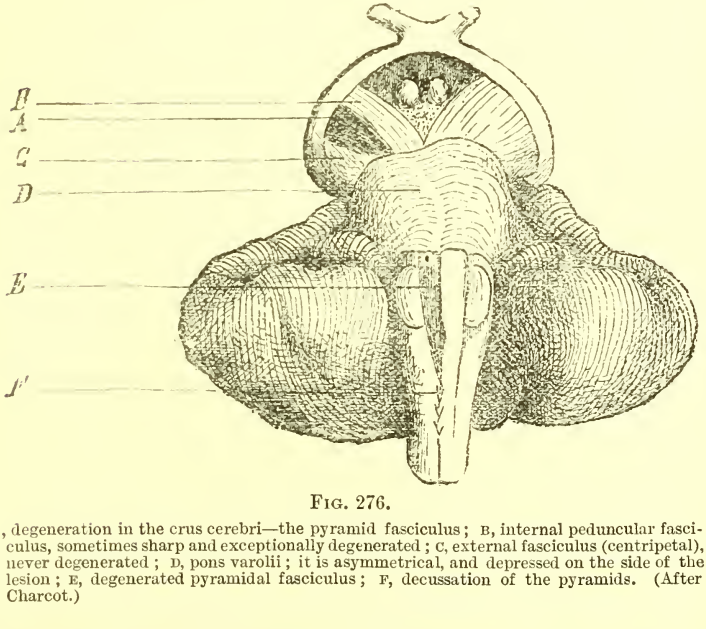

FIG. 276.

A, degeneration in the crus cerebri—the pyramid fasciculus; B, internal peduncular fasciculus, sometimes sharp and exceptionally degenerated; C, external fasciculus (centripetal), never degenerated; D, pons varolii; it is asymmetrical, and depressed on the side of the lesion; E, degenerated pyramidal fasciculus; F, decussation of the pyramids. (After Charcot.)

They have been confirmed by pathology. Every time that a focus of softening or hæmorrhage occurs, implicating and destroying a part of the brain in the form of a truncated pyramid, the base of which is formed of the ascending frontal and parietal convolutions and the paracentral lobule, and the apex by the two anterior thirds of the posterior part of the internal capsule, the motor fibres derived from this part of the brain, and which pass into the spinal cord, are there found to be degenerated. The crus cerebri on the side of the lesion is grey and atrophied; the pyramid continuous with it shows the same atrophy and colour, and the olivary body is more exposed than at the same level on the opposite side (*vide* fig. 276). Below the decussation of the pyramids, sections of the medulla show double degeneration, on the same side as the cerebral lesion in front, near the anterior median fissure (*a*, A, fig. 275, and B, fig. 277), and on the opposite side in the lateral column for a variable distance. Softening of the lateral fasciculus is localised in the most posterior part of this column, between the collateral posterior fissure and the dentate ligament (*vide* fig. 275, *b*, *b′*, *b″*, and A, fig. 277).

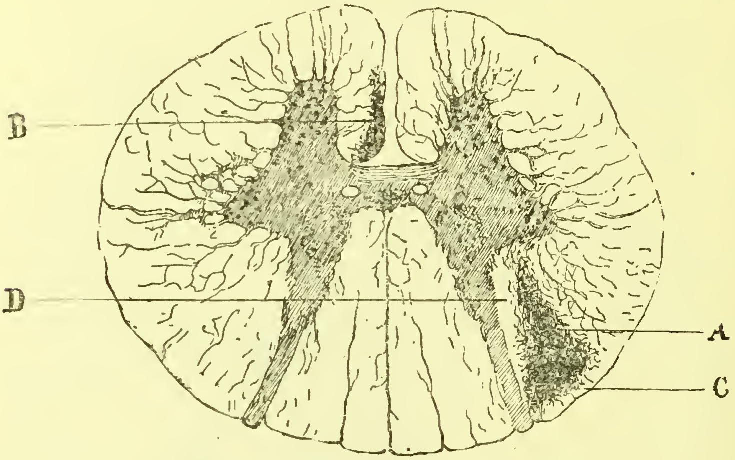

FIG. 277.—TRANSVERSE SECTION OF THE SPINAL CORD IN THE CERVICAL REGION.

A, degeneration of the decussated pyramidal fasciculus in a case of lesion of the motor centres of the cerebral hemispheres; B, degeneration of the direct fasciculus; C, white substance corresponding to the cerebellar fasciculus; D, intermediate region between the posterior horn and the pyramidal fasciculus; this region is always respected in descending degeneration. (After Charcot.)

These secondary degenerations of the spinal cord were first described by Türck, and afterwards verified by Gubler, Charcot, Vulpian, Bouchard, etc. When secondary degeneration is very marked, it may be recognised in a section of the spinal cord in the fresh state, by a change of colour of the white substance, which has become grey and yellowish; but, in order to localise exactly the seat of the degeneration, sections must be cut after having been hardened by the classic method of Lockhart Clarke.

In preparations made in the fresh state, numerous uninucleated granular bodies are found, either free or contained in the perivascular sheaths; atrophy or almost entire disappearance of the nerve tubes is also seen. In cases in which the disease has been of long duration, the granular bodies are less numerous, but there is a much larger number of fibres and cells of the neuroglia and embryonic cells than in the normal condition—in a word, chronic inflammation of the spinal cord is present. This atrophy of the pyramidal fasciculi may be followed by atrophy of the motor cells of the anterior cornua.

Where these spinal lesions are present, recovery of mobility on the paralysed side is impossible, permanent contraction of the extremities—*consecutive contracture of hemiplegia*—is produced, and always accompanies secondary degeneration of the pyramidal fasciculi (Bouchard). It may be remarked that hæmorrhage or softening of the brain, occupying other regions than those indicated above, do not cause secondary degeneration of the spinal cord.

Secondary degeneration following myelitis or loss of substance of the spinal cord.—In Pott's disease, the spinal cord, compressed and irritated by the inflammatory products which are formed around it, undergoes complicated lesions. Tumours, developed either in the spinal meninges or in the vertebræ, may produce the same effects. The spinal cord is then softened, opaque, of a whitish or yellowish tint, for an extent corresponding to the tumour, that is to say, for a limited horizontal segment. When such a segment is destroyed, the spinal cord above and below undergoes changes, which, in the cases examined by Türck, Charcot, Vulpian, Bouchard, and by ourselves, seem to be constant, and are as follows: the posterior columns degenerate above the softened spot (*vide* fig. 278), and the lateral columns below. In the posterior columns the lesion soon becomes localised in the columns of Goll, which are degenerated throughout their whole length and thickness, as far as the floor of the fourth ventricle (*vide* fig. 278). The descending lesion first invades, near the focus of softening, the whole extent of the antero-lateral columns (*vide* fig. 275, D), it then becomes limited to the most posterior part of the lateral columns, near the posterior cornua (fig. 275, E, c', and F, c''): it never affects the cortex of the cord. The degenerated portion becomes less and less extensive as it descends. In the degenerated parts are found nerve tubes which have undergone fatty degeneration and atrophy, and between them numerous granular bodies.

Degeneration of the spinal cord in consequence of compression of the nerves of the cauda equina by a tumour.—In a case of sarcoma of the cauda equina, observed by ourselves, the nerves were compressed and degenerated at the level of the tumour, and the posterior columns of the cord had undergone similar degeneration (fig. 279). Several other cases, since observed, show that the columns of Goll undergo degeneration, in consequence of compression of the nerves of the cauda equina.

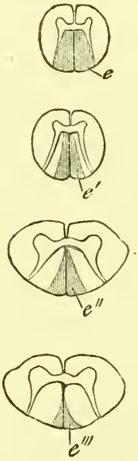

FIG. 278.—ASCENDING DEGENERATION OF THE POSTERIOR FASCICULI OF THE SPINAL CORD, IN A CASE OF COMPRESSION OF THE SPINAL CORD AT THE LOWER PART OF THE DORSAL REGION.

e, lesion of the posterior columns at the dorsal region above the spot compressed; e', a more limited lesion above; e'' and e''', lesions less and less extensive as the cervical region is approached.

To the question **what is the cause of secondary degeneration,** ascending in the posterior columns, and descending in the lateral columns, it may be answered, that nerve tubes divided in any part of their course become granular in that part which is separated from their trophic centre. The experiments of Waller proved that, on dividing the anterior or motor roots of the spinal nerves, the peripheral part of the motor nerves undergoes degenerative change, while the central portion, by preserving its connections with the nerve cells of the anterior cornua of the cord, remains normal. The same observer showed that degeneration of the nerves took the reverse course when the posterior roots were cut; the end which remains connected with the spinal ganglion is normal, while the central segment becomes granular. The morbid changes, observed in the nerve tubes of the spinal cord in secondary degenerations, have been explained by separation from their trophic cells. There is, however, still much obscurity in this subject, due to the fact that the course of the nerve fibres in the spinal cord is far from being perfectly elucidated. In their first physiological experiments, Vulpian and Westphal did not succeed in reproducing ascending and descending lesions in the spinal cord of guinea-pigs and pigeons, by destruction of a portion of the spinal cord; but in more recent experiments, performed on dogs, they observed phenomena of degeneration similar to those observed in man. Schiefferdecker, having succeeded in keeping alive for several weeks dogs in which he had divided the spinal cord at the level of the twelfth dorsal vertebra, also always observed the ascending and descending lesions of degeneration.

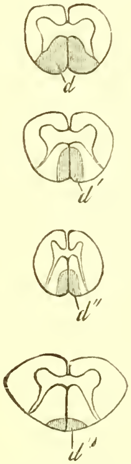

Fig. 279.—Secondary Degeneration of the Posterior Fasciculi of the Spinal Cord, from a case of Compression of the Nerves in the Cauda Equina.

d, lesion of the posterior column in the inferior part of the lumbar enlargement; *d′*, the same lesion at the superior part of the lumbar enlargement; *d″*, lesion at the dorsal region; *d‴*, the same lesion much diminished in extent at the cervical enlargement.

There were traces of morbid change at the end of the first week, and the most complete degenerative changes were attained at the end of four or five weeks. Ascending degeneration was found, as in man, in the columns of Goll and in the direct cerebellar fasciculi; descending degeneration was very apparent in the antero-lateral columns.

There is in man, however, an exception to secondary degeneration of the spinal cord. In the disease, to be described presently, called *sclerosis in plaques*, in which the grey centres and white fasciculi of the cord are irregularly destroyed, no secondary degeneration of the nerve tubes is observed. Vulpian concludes from this that secondary degeneration is not alone caused by separation of the nerves from their cells, but that persistent irritation plays an important part in these changes. We may add, in conclusion, that on examining the spinal cord of subjects who had suffered amputation a long time previously, or of animals in which the sciatic nerve had been divided, the consecutive lesions of the spinal cord were found to implicate not only the white posterior columns but also the anterior columns and the cells of the anterior cornua (Vulpian).

Myelitis.—Under this name may be described a series of very different pathological conditions, in which there is acute or chronic inflammation of the various elements of the spinal cord. Indeed, under the name of myelitis is included not only uncomplicated inflammation, characterised by the formation of new elements, embryonic cells, white blood corpuscles, or pus cells effused between the elements of the spinal cord, but also multiplication of the elements and thickening of the neuroglia, known as sclerosis. Reasoning from the same sequence of facts, atrophy of the nerve elements, which in certain cases of poliomyelitis is the only lesion found at the autopsy, would be referred to inflammation.

Myelitis may be acute or chronic. According to the classification given by Vulpian, and generally adopted, we divide myelitis into diffuse or systematic. Myelitis is said to be systematic when limited to a column of either white or grey substance and when it has a regular evolution. Acute and chronic, diffuse and systematic, myelitis will now be studied in order.

A. Acute Myelitis.

a. **Acute diffuse suppurative myelitis** is very rare ; it may be met with in epidemic spinal meningitis, and in consequence of eschars of the sacrum having invaded the membranes of the spinal cord ; the myelitis is then superficial and consecutive to meningitis. In certain cases of gangrenous eschars observed in the insane, the purulent exudation and the inflamed spinal meninges, as well as the cord itself, have all the characters, the colour, and odour of gangrene : these lesions may extend to the medulla oblongata, the pons varolii, and the base of the brain. Metastatic abscesses are seen exceptionally in the spinal cord in the case of purulent infection.

b. **Diffuse simple acute myelitis** has various causes—wounds, chills, meningitis, tumours of the meninges, acute infectious diseases, such as typhoid fever, variola, etc. The lesions are sometimes limited to a very small extent of the spinal cord, and at others occupy almost its whole length. Its naked-eye appearances are variable ; sometimes the spinal tissue is softened, whitish, pink, yellowish, or brown in colour, according as the blood-vessels are more or less congested, or as the red corpuscles are extravasated in greater or less numbers ; sometimes ecchymotic spots and dilated vessels are seen ; in other cases the spinal cord is on the contrary rather hardened than softened, and on microscopic examination there are found granular nerve tubes, a large quantity of white corpuscles, some of which are normal, others filled with blood, pigment cells, and free fat granules, and granular bodies : the latter are found in the perivascular sheaths. When the spinal cord is softened, microscopical examination is not possible in the fresh state ; if, however, it has preserved a certain consistence, it may be hardened by the usual methods, and examined in delicate sections. In such preparations the state of the blood-vessels, their dilatation, the fibrinous exudations, the effusion of lymph cells into the perivascular sheaths, and the new formation of nuclei and small cells in the grey cornua and commissures, may be recognised ; the stellate or Deiters cells are more numerous and more apparent than in the normal condition.

The nerve cells of the anterior cornua sometimes undergo extreme hypertrophy in acute myelitis (Charcot); they may even measure 80 μ in diameter; they are filled with an amyloid substance, vitreous in appearance, and in which one or more vacuoles filled with blood may be recognised; the nucleus of these cells is more or less modified, their nucleolus has often disappeared, and they themselves may be either transparent or granular. Alongside these hypertrophied cells others are found, which are hardened, atrophied, without nuclei or processes, irregular in shape, and staining badly with carmine, or else transformed into masses of small granules. The axis cylinders are hypertrophied, varicose, and granular, or excavated with vacuoles. (Frommann, Charcot and Joffroy, etc.) This state of the axis cylinders was observed by Joffroy in myelitis produced experimentally in the dog.

Foci of granular disintegration (Lockhart Clarke), in which all the nerve elements are reduced to granules, have also been described in myelitis. As these foci have been seen in spinal cords, the freshness, careful preparation, and hardening of which may be suspected, it seems probable that they are often the result of accident, and are really artificial changes.

The lesions of acute myelitis are distributed in a very varying manner; in some cases they predominate in the grey central part of the spinal cord; in others the cortex is more particularly affected, especially when myelitis is consecutive to meningitis or to a tumour of the meninges; sometimes they are localised in only one half of the spinal cord. Inflammation of the meninges, and degeneration or interstitial inflammation of the roots of the nerves near the diseased parts, are generally present at the same time. Hæmorrhage may be, according to Charcot and Hayem, the consequence of inflammatory softening; the effusion of blood which is then produced hastens the fatal termination. Localised myelitis is, on the contrary, followed by ulterior changes, such as complete degeneration and atrophy of the parts in which it is seated. It is then undistinguishable from limited chronic softening.

c. **Acute ascending paralysis.**—These cases of diffuse acute myelitis are closely related to those described by Landry, and since called by the name of acute ascending paralysis. At the autopsy of persons affected with this disease, which runs the same course as very acute myelitis, no lesions, either gross or microscopic, can be discovered in the spinal cord. In the autopsies made by Landry, Vulpian, Lévy, Hayem, Déjerine, Westphal, and by ourselves, no lesions were discovered capable of explaining the paraplegic symptoms. It should not however be concluded that no lesions exist, but only that hitherto they have escaped our methods of investigation. It should be added, however, that in two recent observations made by Reinhard and Eisenlohr, spinal lesions, corresponding to a very mild degree of myelitis, were found, namely, swelling of the axis cylinders and motor cells, fibrinous exudation round the blood-vessels, and capillary hæmorrhages. Déjerine found these lesions in the anterior roots of the spinal nerves in two cases of ascending paralysis; the nerves presented the same lesions as are observed in the peripheral segment of a divided nerve. Déjerine thought that these alterations of the nerves were consecutive to a lesion of the cells of the anterior cornua, which lesion, however, he did not find. It is therefore necessary to wait before deciding as to the value of the lesions hitherto described; they do not appear to us to be in proportion to the serious nature of acute ascending paralysis.

d. **Acute systematic myelitis.**—Acute systematic myelites are not numerous, and are limited entirely to the anterior cornua of the spinal cord. The myelites of the anterior cornua, still called systematic anterior poliomyelitis, form a natural group, on which much light has been thrown of late years by Duchenne, Charcot, Joffroy, Damaschino, etc. They comprehend the spinal paralysis of infants, the spinal paralysis of adults, and progressive muscular atrophy. The myelitis of infantile paralysis is acute, the spinal paralysis of the adult is subacute, and progressive muscular atrophy pursues a chronic course. The common phenomena of these polio-myelites are that motion and the voluntary muscles are alone affected, the sensibility remaining intact, and that they are accompanied with trophic troubles, chronic fatty degeneration, and atrophy of the muscular fibres.

The lesions found after death in **infantile paralysis** are various, for, the disease having lasted for a variable length of time, sometimes the lesions of recent myelitis are found, and at others atrophic changes, which originated many years previously. Thus in the autopsy of a patient of Charcot, in which one of us made a microscopical examination of the spinal cord, and showed for the first time (1863) that there was a positive lesion, the paralysis had existed forty-seven years; there was very pronounced atrophy of the antero-lateral columns, which contained a considerable number of amyloid corpuscles. Prévost and Vulpian described the lesion of the anterior cornua, and the disappearance of the motor cells, in 1865. Lockhart Clarke and Laborde published similar observations at the same time. In 1870 Charcot and Joffroy published a histological analysis of the spinal cord of a woman who had been the subject of infantile paralysis for thirty-eight years. In this case the anterior cornua were profoundly altered throughout almost the whole length of the cord; the motor cells were atrophied, and groups of them had entirely disappeared. The substance of the anterior cornua was sclerosed in places, but the connective tissue was not equally altered everywhere; finally, the anterior columns were atrophied and partially sclerosed, as well as the roots of the anterior nerves. These observations showed the distant anatomical consequences of infantile paralysis, but not the myelitis of its commencement. Roger and Damaschino, Dujardin-Beaumetz, Roth and Leyden, have published cases in which the lesions were recent, and the foci of myelitis were characterised by the presence of granular bodies, and by sclerosis of the anterior cornua, accompanied with atrophy of the motor cells, and atrophic degeneration of the lateral columns and the anterior roots. Thus at the present time the pathological anatomy of infantile paralysis is perfectly well defined in its most important points.

Acute spinal paralysis of the adult corresponds entirely by its lesions, as well as by its symptoms, with infantile paralysis, but cases followed by autopsy and complete examination of the spinal cord are still very rare. We know of no observation thoroughly made but that of Gombault's, in which atrophy of the nerve cells of the anterior cornua was present. In an autopsy Leyden found a cystic focus in the lumbar enlargement of the cord, in the right anterior cornua, due to hæmorrhagic softening, and near it the motor cells were atrophied.

B. Chronic Myelitis.

Under the name of chronic myelitis are included a series of pathological states of various origin, which are far from presenting similar anatomical characters; thus, the lesions of softening of the spinal cord, described above, the various sequelæ of acute myelitis, such as atrophy of the nerve tubes and cells, the formation of new connective tissue in the grey and white centres of the cord, the cysts and foci which follow softening or circumscribed hæmorrhagic myelitis, the inflammation and softening, caused by lesions of the meninges and vertebræ in Pott's disease, vertebral cancer, and the cortical leuco-myelitis which result, and the subacute or chronic cortical myelitis, which so often accompanies general paralysis of the insane, form so many distinct chapters in a complete description of chronic myelitis. But the histological lesions met with in these pathological conditions, so different in their causes, are actually the same, and may be all included in the general description which we have already given of softening and acute myelitis, or in that of sclerosis, which still remains for us to furnish. Chronic spinal myelitis is in fact generally interstitial myelitis or sclerosis.

Interstitial myelitis or sclerosis of the spinal cord.—When a part of the spinal cord is affected with sclerosis, a lesion which generally occupies systematically either certain fasciculi or irregularly distributed patches, the diseased parts may be recognised with the naked eye by their grey or greyish-yellow tint, and by their semi-transparency. This semi-transparency, which is quite characteristic when present in the white fasciculi, is due to the fact that the nerve tubes have lost their myelin without the nervous tissue being infiltrated with opaque elements. The nerve tubes are reduced to their axis cylinders, and the tissue of the neuroglia thickening around them, the fibrils of the connective tissue resemble the nerve tubes, and are undulated so as to appear thicker. This kind of condensation of the fasciculi of the fibres of the neuroglia, which coincides with a diminution in the diameter of the nerve tubes, almost always causes, particularly if the lesion is old, an actual thickening of the connective-tissue fasciculi which radiate from the centre of the cord to its periphery in company with the blood-vessels, thus the fasciculi of the cord are separated by thicker septa than what normally divide the nerve tubes from one another. The cells of the neuroglia are easily isolated; they contain one large nucleus. In the cornua of the spinal cord sclerosis manifests itself, at first by a greater abundance of small cells, and afterwards by a new formation of fibrils of connective tissue, at the same time that the nerve cells, at first tumefied and granular, as in all myelites, gradually atrophy and finally disappear.

In the ultimate stages of sclerosis, the septa which separate the nerve tubes—reduced to their axis cylinders—and the fasciculi of tubes, are gradually thickened, and are always formed of fibrils. The cells of the neuroglia are smaller than at the commencement

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of the process, and they do not always seem to be increased in number. Throughout this tissue amyloid corpuscles are found, more particularly alongside the fibrous septa. At the same time the capillary vessels and the small arteries and veins contain granular bodies in their perivascular sheaths, or in their external coats; later, their walls undergo thickening.

This interstitial myelitis may be compared to chronic inflammations of the same nature, observed in the liver, kidneys, and lungs; but it differs from it in many respects, quite as much as the connective tissue and extremely delicate fibres of the neuroglia differ from bundles of fasciculated connective tissue. In sclerosis of the spinal cord, thickening and new formation of connective-tissue fasciculi, comparable by their extent, thickness, and importance to those found in cirrhosis of the liver, or in interstitial pneumonia, must not therefore be looked for.

With the exception of sclerosis in plaques, all chronic sclerotic myelites belong to the group of systematic myelites. We shall therefore describe in order chronic anterior poliomyelitis, which corresponds to progressive muscular paralysis; bulbar progressive paralysis, or labio-glosso-pharyngeal paralysis; sclerosis of the posterior cords, or progressive locomotor ataxy; amyotrophic lateral sclerosis, or spasmodic paraplegia, and sclerosis in plaques.

a. **Chronic anterior poliomyelitis.**—Paralysis, or progressive muscular atrophy, has been long regarded as the result of primary atrophic fatty degeneration of the muscles. Cruveilhier, however, observed in an autopsy of this disease a very remarkable atrophy of the anterior roots (1853).[1] Vulpian,[2] Trousseau, and Jaccoud also ascertained that the anterior roots were thin and grey in this disease. Later, Schneevogt[3] and Jaccoud[4] discovered that the cervical trunk and part of the abdominal cord of the sympathetic were altered in this disease. Many other observers noticed ill-defined lesions in the spinal cord; Luy[5] discovered atrophy of the cells of the anterior cornua; Lockhart Clarke, 1868, observed atrophy of the multipolar cells of the spinal cord; but the pathological anatomy of the disease was only

[1] *Bulletin de l'Acad. de méd.*, t. xviii. no. 12, p. 546.

[2] *Soc. méd. des hôpitaux*, Mars 1863, and *L'Union médicale*, 1863, no. 49, t. xviii. p. 159.

[3] *Neederl. Lancet*, 1854, Sept. and Oct.

[4] *Soc. méd. des hôp.*, 1865, and *Gazette des hôp.*, 1865, p. 20.

[5] *Gazette méd.*, 1860, p. 30.

established when Charcot and Joffroy[1] published their memoir, which was based on cases studied in the Salpêtrière, as well as in Charcot's and Vulpian's wards.

Considering these cases in connection with those already published, it was found that the constant and essential lesion of progressive muscular paralysis is atrophy of the cells of the anterior cornua of the spinal cord, followed by their complete disappearance. The grey substance of these cornua is also diminished in size and sclerosed, and the anterior roots are atrophied and degenerated. The regions of the cord affected are more or less extensive, the nuclei of Stilling and the medulla oblongata may be affected as well as the motor centres of the spinal cord. Another spinal lesion, which is often coincident with progressive muscular atrophy, is the formation of a central cavity in the cord, or hydromyelia (cases reported by Clarke, Schüppel, and Grimm, quoted by Leyden).

b. **Progressive bulbar paralysis.**—The lesions of progressive bulbar paralysis, or **labio-glosso-pharyngeal paralysis,** are the same as those of progressive muscular paralysis, and do not differ except by the muscles affected, and by the seat of the morbid changes in the nerves and centres. In this disease it is particularly the muscles of the tongue which are atrophied, and in a state of fatty degeneration. The trunks of the facial, hypoglossal, pneumogastric, and spinal nerves are more or less affected by granular degeneration, implicating particularly the nerve tubes, and they finally show the lesions of sclerosis with atrophy. The anterior cornua of the cord, and the grey centres of the medulla oblongata, are modified in the same way as in progressive muscular atrophy. The atrophy of the nerve cells is most marked in the deep origins of the hypoglossal, spinal, and facial nerves; complete disappearance of the cells is the final result. The atrophy may also affect the nuclei of origin of the glosso-pharyngeal and the pneumogastric, which are mixed nerves. The intrabulbar nervous fasciculi, particularly the transverse fasciculi of the medulla oblongata, are more or less atrophied at the same time.

Sclerosis of the posterior cords. Locomotor ataxy.—Sclerosis, or grey atrophic degeneration of the posterior cords, corresponding to progressive locomotor ataxy, offers us one of the most remarkable examples of the progress made in nervous pathology during the last thirty years. The symptoms of this disease, separated from those of paraplegia and sclerosis by Duchenne of Boulogne, its pathological anatomy elucidated by Cruveilhier, described by Bourdon and Luys, Charcot and Vulpian, Axenfeld, Jaccoud, Leyden, Pierret, etc., have now established a perfectly well-known type, recognisable still in its unusual localisations and in its abnormal forms.

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[1] *Arch. de phys. norm. et path.*, 1869, p. 356.

On examining a spinal cord affected with this disease, the pia mater is almost always found to be thickened and adherent to the posterior columns, which appear transparent through this membrane; and on making a transverse section, the posterior columns are seen to be of a peculiar transparency and of a grey colour. Two phases may be distinguished in the course of this disease: at the commencement there is an increase in the number of the elements of the neuroglia, and the diseased parts appear slightly tumefied; in the second stage there is, on the contrary, atrophy of the cellular elements of the neuroglia, thickening of its fibrous tissue, and atrophy of the nerve tubes. On examining under the microscope a small fragment of the semi-transparent grey substance of the diseased part in the first period, and in the fresh state after soaking in water, a rather considerable number of embryonic cells are at first seen imbedded in a granular amorphous substance; the nerve tubes are preserved as well as the nerve cells of the anterior and posterior cornua; the perivascular sheaths of the blood-vessels of the morbid part are dilated and filled with granular lymph cells.

To obtain a complete idea of the lesion, the spinal cord should be hardened in weak chromic acid or in Müller's fluid, and it is essential that it should not be dragged or pressed between the fingers. The hardening effected, transverse or longitudinal sections are cut, stained with carmine, treated with absolute alcohol, then cleared with essence of turpentine or oil of cloves, and preserved in Canada balsam or Damar resin. In such preparations the diseased parts are seen to be more highly coloured than the healthy fasciculi, for they contain more elements which fix the carmine; thus, even with the naked eye, the extent of the lesion can be recognised in transverse sections which have been hardened in chromic acid and stained with carmine. On microscopically comparing delicate sections of healthy fasciculi with those of the diseased posterior columns, it will be seen that in the first the divided nerve tubes are regularly separated from one another by delicate septa of the neuroglia, and by blood-vessels (*vide* B, fig.

280), and here and there a few small cellular elements are found in the neuroglia ; in the posterior columns the nerve tubes are, on the contrary, of various diameters, some are very small, though still retaining their axis cylinders and an envelope of myelin, others are of normal size or even larger than in the healthy condition, their axis cylinders being often considerably hypertrophied. Between the nerve tubes tracts or masses of small cells of the neuroglia are seen, the nuclei of which are only visible when the method of preparation given above is employed. Longitudinal sections of the spinal cord show similar histological details in every way comparable.

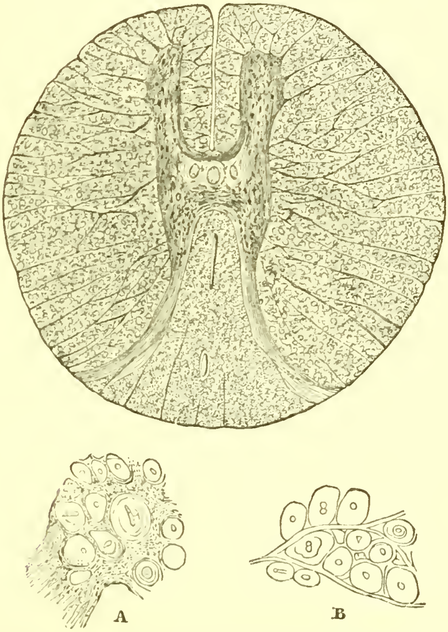

Fig. 280.—Section of the Spinal Cord in Locomotor Ataxy—Grey Atrophic Degeneration or Sclerosis of the Posterior Columns.

The fig. C represents a complete section of the spinal cord ; the part comprised between the posterior cornua is seen to be altered, and appears under this low power (10 diameters) to be more finely granular than the lateral columns. The posterior columns are united so that the posterior median fissure is abolished ; B, transverse section of healthy lateral columns ; A, transverse section of diseased posterior columns in which the neuroglia is thicker and fibrillated.

In a more advanced stage of the disease the posterior columns are united together by the formation of new connective tissue, which fills up the posterior fissure (*vide* fig. 280). This connective tissue, which plays the part of cicatricial tissue, intimately unites the two columns of Goll, which before were simply placed side by side. In consequence of these changes, the posterior columns become considerably atrophied. Transverse sections under a high power show that the nerve tubes are separated by very fine connective-tissue fibrils, intersecting in every direction. (A, fig. 280). In the midst of these fibrils a few nuclei are seen. The nerve tubes are thin, but their axis cylinders are always preserved. Some observers have asserted that the nerve tubes have disappeared by the time sclerosis has reached this stage; but as a matter of fact they may be always found, when sections are well made and stained with carmine; when the lesion is far advanced, the tubes may be reduced to their axis cylinders, the medullary sheath having completely disappeared. The walls of the capillaries and small blood-vessels are thickened and rigid, and their calibre diminished; a large number of amyloid corpuscles are at the same time found in their course as well as in the tissue of the neuroglia, especially beneath the pia mater. The posterior roots of the spinal nerves become transparent, and so small that, instead of being, as in the normal condition, double the size of the anterior roots, they may be only half their diameter, or even less.

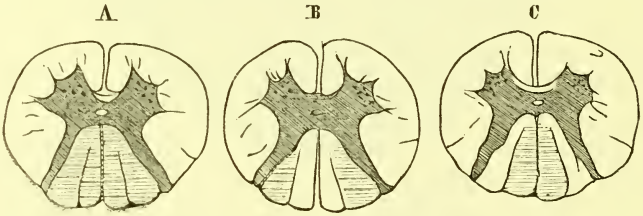

FIG. 281.

A, sclerosis of the whole of the posterior columns—the columns of Goll and the radicular zones are simultaneously altered (common locomotor ataxy); B, sclerosis of the two posterior radicular zones, the columns of Goll being respected (locomotor ataxy at its commencement); C, sclerosis limited to the columns of Goll; ascending degeneration. (After Charcot.)

In locomotor ataxy the lesion is not always limited to the posterior columns; it encroaches sometimes a little on the cortical substance of the contiguous lateral columns, in which case new symptoms of paralysis occur related to these lesions. The lesion of the posterior columns is generally more advanced and older in the lumbar region than in the dorsal or cervical regions, where the lesions are almost always less marked. The tubercula quadragemina, the optic tracts, the optic nerves themselves, may be atrophied, greyish, and semi-transparent; sometimes even the hypoglossal nerve and the auditory nerve show the same atrophy.

The characteristic symptoms of ataxy are due, not as was formerly thought to a lesion of the whole of the posterior columns, but only to sclerosis of the radicular or cuneiform columns. In several observations, the first of which was published by Pierret, only the fasciculi of these columns were altered which are adherent to the posterior cornua ; the lesions of the columns of Goll being simply consecutive, and caused by ascending degeneration. In the majority of autopsies of locomotor ataxy hitherto published, the radicular fasciculi and the columns of Goll are affected in the same degree. The cells of the spinal ganglia and of the grey centres of the cord are perfectly normal in most cases.

Amyotrophic lateral sclerosis.—In 1866 [1] Charcot published the first clinical case referred to symmetrical sclerosis of the lateral cords ; since then a definite symptomatic type, called spasmodic paralysis, has been defined, based on a series of new cases collected by Gombault,[2] Joffroy, Debove, etc. The histology of sclerosis, or grey degeneration of the lateral columns, is exactly similar to that of locomotor ataxy, hence there is no occasion to redescribe it. Its seat corresponds exactly to the course of the pyramidal fasciculi, and is the same as that of descending degeneration (*vide* p. 612). The lesion commences in the medulla oblongata on each side of the olivary bodies, and after decussation of the pyramids, it is seen on each side of the spinal cord as two spots at the most posterior part of the lateral fasciculi, and at the inner side of the anterior columns. It becomes more and more attenuated as the lower parts of the cord are reached. When very marked it is easily recognised on the surface of the spinal cord, through the pia mater, even with the naked eye. When the spinal cord has been hardened and sections cut and stained with carmine, the diseased spots are easily recognised by the red stain they take.

Charcot distinguishes two stages in this disease: in the first the white columns are alone affected; in the second the multipolar cells of the anterior cornua are atrophied and deeply pigmented, the lateral nerve cells and the columns of Clarke remaining intact. The cells of the grey nuclei of the medulla oblongata are often altered and atrophied. The roots of the anterior spinal nerves, and the nerves themselves, are degenerated when the motor cells are affected, and the muscles to which they are distributed are atrophied. These lesions, which closely connect amyotrophic lateral sclerosis with progressive muscular atrophy, induce many pathologists, Leyden among others, to deny to amyotrophic lateral sclerosis a distinct pathological entity.

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[1] *Bulletin de la Société méd. des hôpitaux*, 1866, pp. 24–31.

[2] Gombault, *Etude sur la sclérose amyotrophique* (thèse de Paris, 1877).

Sclerosis in disseminated plaques.—This disease differs from all the preceding by its irregularity, and by the fact that it is not systematically localised in any spinal fasciculus. Cruveilhier described this sclerosis in his atlas, but it remained simply a curiosity till Leyden (1863),[1] Rindfleisch, Vulpian, and Charcot, by careful autopsies compared with clinical observations, were enabled to give a complete account of the disease.[2]

On the surface of the spinal cord and the medulla oblongata, semi-transparent grey patches are seen, varying both in extent and number ; they may be from 2 to 70 cm. in length, and are asymmetrical, irregular, and occupy indiscriminately the various white columns and grey centres of the spinal cord. They are sometimes unilateral, or more marked on one side than on the other ; but their extent and limits are often difficult to appreciate with the naked eye. Thus, in order to determine exactly the parts affected, and to what degree, the spinal cord must be hardened and examined in sections, stained with carmine and mounted in Canada balsam. Such preparations, examined under the microscope, show that the sclerosed tissue presents all the characters already indicated as typical of sclerosis in general, and of sclerosis of the posterior columns in particular ; the same thickening and condensation of the neuroglia is seen, the stellate cells of Deiters are sometimes very numerous, and the nerve tubes have more or less lost their medullary sheaths. The nerve cells included in a plaque resist for a certain time, but they ultimately become infiltrated with numerous yellow granules, a state corresponding to their exaggerated pigmentation ; they then retract, take on a shiny appearance, and finally atrophy, and may even completely disappear. The lesions of the spinal roots and nerves are related to those of the nervous centres. With regard to their location, sclerosis in plaques is sometimes cerebro-spinal, sometimes purely spinal.

In **tetanus** Demme has described lesions similar to those of sclerosis, and which at their commencement are disseminated throughout the whole cord. In tetanus Michaud has described hypertrophy of the elements of the neuroglia of the grey commissure and round the central canal. We ourselves have examined a certain number of the spinal cords of subjects who have died from traumatic tetanus, but we have never been able to discover a single morbid change.

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[1] *Deutsche Klinik*, 1856.

[2] *Vide* Ordenstein, *La paralysie agitante et la sclérose en plaques généralisées* (thèse de Paris, 1867).—Bourneville, *Scléroses en plaques généralisées* (*Mouvement méd.*, 1868).

Central or peri-ependymar sclerosis. Cystic formations in the centre of the spinal cord.—A small number of cases have been reported in which the connective tissue surrounding the central canal of the spinal cord was thickened, transformed into an elongated fibrous plaque, or into a positive tumour situated alongside the central canal: this was particularly the fact in a case quoted by Lancereaux. At the same time that this thickening of the peri-ependymar tissue takes place, the central canal of the spinal canal is almost always found to be more or less dilated, and filled with fluid for a variable extent. The fibrous plaque is generally continuous with the extremity of one of these dilatations, or it is seated in the wall of the abnormally dilated cavity. These dilatations have been variously explained. Hallopeau[1] looks upon them, and the new formation of the peri-ependymar connective tissue, as the simple result of myelitis. Th. Simon[2] and Westphal found the longitudinal cystic cavity to be in similar cases quite distinct from the central canal, and situated behind it in the posterior columns. In the case recently published by Schüppel, and reported by Leyden,[3] this cavity extended so far into the posterior columns as to almost completely destroy them. According to these authors, this condition was not due to central myelitis, but to tumours, belonging to the class of glioma or gliosarcoma, developed around the canal of the ependyma, and containing in their interior cysts which were continuous or not with the central canal. The presence of these tumours in the midst of the spinal cord might become the starting-point of inflammatory lesions of this organ. In some cases, in which the cystic cavity has been observed alongside the central canal, the former might have been developed at the expense of the latter, for Vulpian has in the same spinal cord observed two cavities placed side by side, one was dilated and transformed into a cyst, while the other remained normal.

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[1] *Arch. gén. de méd.*, 1871 and 1872, and *Nouveau Dic.* t. xvii. p. 461.

[2] *Beiträge zur Path. und Path. Anat. des centralen Nervensystems* (*Arch. f. psych. und Nerven-Krankheiten*, Bd. v. i. p. 108).

[3] *Traité clinique des maladies nerveuses*, French trans., 1879, p. 693.

Tumours of the spinal cord.—Tumours of the spinal cord are rare, and are generally located in the meninges; they do not differ from tumours of the brain and the cerebral meninges. Lancereaux has observed a **fibrous tumour** developed in the central canal of the cord, and occupying a part of its length; we have also seen a small fibroma developed in the pia mater of the spinal cord. **Neurogliac** and **angiolithic sarcoma** may be found in the spinal meninges. We have already described **tubercle** of the meninges (*vide* pp. 580 and 606). A very small number of indisputable cases of syphilitic **gummata** of the spinal cord have been reported: they resemble those of the brain (*vide* p. 600).

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On page 85 will be found the titles of the principal treatises on general pathological anatomy. The following is a list of the principal works on each division of the subject as classified in this manual.

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